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THE UNIVERSITY OF TORONTO
MEDICAL JOURNAL
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EDITORIALS

A RENEWAL OF AMBITION

Another summer has come, enveloped us in its warmth, and fled. Once again we return to engage in our studies, and to record the sights and sounds it will be our privilege to see and hear during the next eight months.

We say "privilege" advisedly. The study of Medicine is not a right; rather, it is a responsibility granted to those few who qualify through ability and personality. Few of us are sufficiently aware of the magnificent opportunity that has been entrusted to us, and there is a tendency to be almost indifferent to it, while we dissipate our energy in unworthy pursuits.

It is sobering to realize that today there are thousands of students on this continent facing a bleak, uncertain future. Denied acceptance into the medical schools of their choice, they now seek frantically for any college that will accept them. It requires little imagination to picture their frustration, unhappiness, and even despair. How fortunate are we to be members of an excellent medical school!

Although cognizant of their good fortune in being enrolled in Medicine, a number of students, regarding the unrest extant in the world today, feel reluctant to strive wholeheartedly for a goal that might, in a few brief moments, be blasted into nothingness. Such pessimism, it must be confessed, is not without reason; scarcely six years after the conclusion of World War II, the victors are at each other's throat, and a small plot of land is being systematically torn asunder by opposing armies.

What should be remembered, how-

ever, is that periods of darkness have existed in every generation, bringing with them the doubts and uncertainty felt today. Yet, in spite of, or perhaps because of, these episodes, mankind has continued to progress towards better things. Let those who are discouraged, therefore, take heart, and renew their ambition to achieve success in their chosen profession.

"You young men—doctors and scientists of the future—do not let yourselves be tainted by a barren skepticism, nor discouraged by the sadness of certain hours that creep over nations. Do not become angry at your opponents, for no scientific theory has ever been accepted without opposition. Live in the serene peace of libraries and laboratories. Say to yourselves first: 'What have I done for my instruction?' and as you gradually advance: 'What am I accomplishing?' until the time comes when you may have the immense happiness of thinking that you have contributed in some way to the welfare and progress of mankind."

LOUIS PASTEUR.

A SPLENDID GESTURE

Few of the students using the facilities of the Medical Reading Room are aware of the expenses involved in operating this library. As the cost of living has risen, so has the cost of medical literature. Consequently, the Library, with only limited funds at its disposal, has often had to postpone the purchase of needed texts.

It is very gratifying, therefore, that a medical organization, and several business concerns have donated money to the Medical Reading Room for the purchase of books and periodicals. To the College of Physicians and Surgeons, for their two splendid gifts, and to the British Drug Houses, Rexall Drug Co., E. B. Shuttleworth Chemical Co. Ltd., and Canadian Breweries, for theirs, the JOURNAL, on behalf of the undergraduate body, says "Thank you."

FISSION AND THE PHYSICIAN

In this issue of the JOURNAL, we present the first of a series of articles dealing with the relation of Medicine to the Atomic Age. Now that mankind seems bent on employing the energy derived from the splitting of the atom, in war, and perhaps in peace, it is essential that we, as medical men of the future, be aware of all the dangers inherent in radioactivity.

The article this month, written by a medical officer in the Royal Canadian Navy (Reserve), serves as an introduction to the principles that underlie the construction of the "A" Bomb, and outlines some of the major medical problems produced by an atomic attack. In a later issue, the actual clinical effects of radiation will be discussed.

In Memoriam

JACK ZOBERMAN

(1930-1951)

On July 23, 1951, Jack Zoberman, a member of the class of Meds 5T4, drowned while employed at an Ontario summer lodge. The accident was a great shock to all his friends, and a heavy loss to his parents and the community.

Born in Toronto in 1930, he attended Clinton St. Public School and Harbord Collegiate Institute where he established remarkable academic records. It was easily evident that he was an exceptional scholar, and on graduation from high school, not unexpectedly entered Medicine. At the time of his death, he had completed First Medical year, had ranked second in his class in two consecutive years, and had developed a true love for his studies. Had he lived, his future success in the field of Medicine would have been certain.

A scholarship fund has been subscribed to by his relatives, friends, and fraternity brothers in order to perpetuate his relationship with the Faculty of Medicine at the University of Toronto.

PARENTERAL FLUID THERAPY IN PEDIATRICS

EARL KRIEGER, M.D.*

An important subject in pediatrics with which the medical student frequently encounters difficulty, is parenteral fluid therapy. This article is an attempt to resolve for the student some of the complexity of this subject.

This subject will be covered under the following headings:

(1) Fluid and electrolyte balance.
(2) Replacement of fluid and electrolytes.
(3) Routes of administration.
(4) Solutions available and indications for their use.

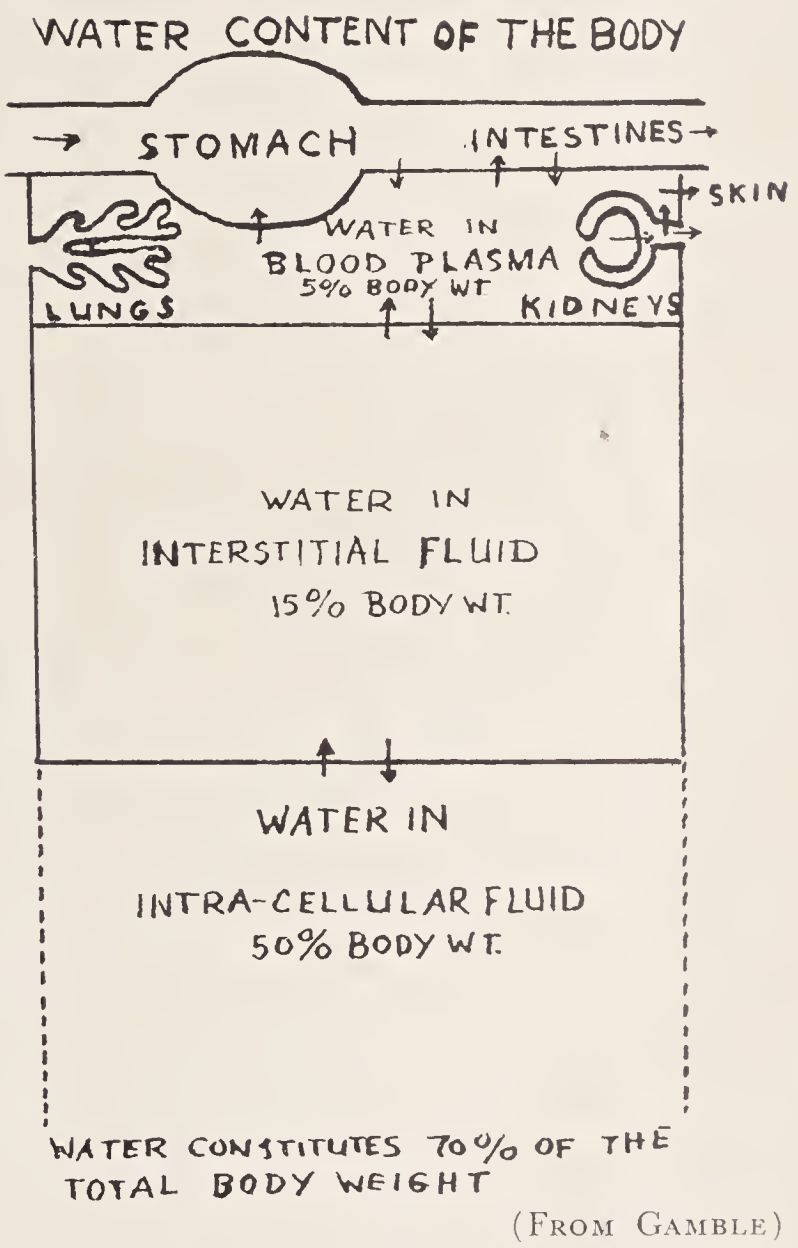
FLUID AND ELECTROLYTE BALANCE

The following highlights represent a review of the basic features of fluid and electrolyte balance.

Table one indicates the way in which fluid is distributed among the body's tissues. Preliminary reports of recent research suggest that the total body water, as measured by the deuterium oxide and antipyrine methods, varies between 53 to 63 per cent in children and between 70 to 83 per cent in premature and newborn infants.

Tables one, two, and three indicate the importance of fluid in body constitution and the fact that the fluid balance in infants can be much more readily disturbed than in adults. Normally about one-half of the total extracellular fluid of the infant is being exchanged every day as compared to about one-seventh of the total extracellular fluid of the adult. The minimal urine volume to cover the excretion of end products of metabolism in a seven kilogram infant is assumed to be 100 cc. and in a 70 kilogram adult is assumed to be 500 cc. Therefore the irreducible urine volume for an infant is assumed to be one-fifth of the value for the ten-times-heavier adult. Vomiting, diarrhea, and the other causes which upset the water exchange—produce a correspondingly greater disturbance in the fluid and electrolyte balance of the infant than they do in the adult.

Table 1



(From Gamble)

*From the Wards and Laboratories of the Hospital for Sick Children under the direction of Alan Brown, M.D., F.R.C.P.(Lond.).

TABLE 2

APPROXIMATE NORMAL WATER LOSSES AND ALLOWANCES PER DAY FOR PERSONS OF VARYING SIZE NOT SUBJECT TO EXERTION OR SWEATING

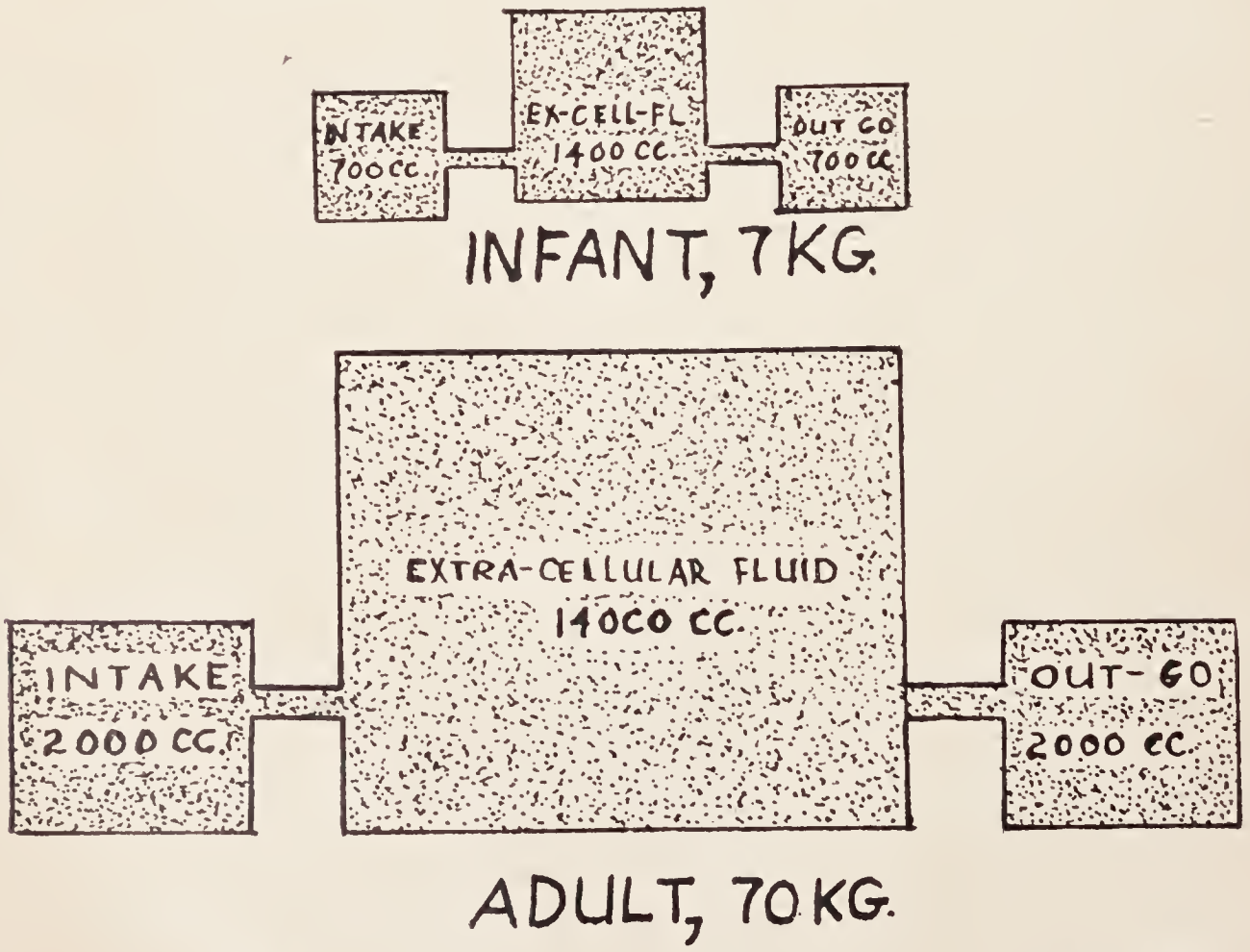
Size	*Water Loss*				*Usual Water Allowances*		
	Urine	Stool	Insensible	Total			
	cc.	cc.	cc.	cc.	cc./person	cc./kg.	oz./lb.
Infant (2–10 kg.)	200– 500	25– 40	75– 300	300– 840	330–1000	165–100	2.5–1.5
Child (10–40 kg.)	500– 800	40–100	300– 600	840–1500	1000–1800	100– 45	1.5–0.7
Adolescent or Adult (60 kg.)	800–1000	100	600–1000	1500–2100	1800–2500	45– 30	0.7–0.5

(FROM BUTLER AND TALBOT)

Table four indicates, on the left side, normal values for the cations and anions of the blood plasma and illustrates their relative magnitude on the right side. The solid line in the diagram indicates the practically complete dissociation of the salts in the blood plasma into separate ions. The dissociation of carbonic acid is the only exception since its dissociation is only slight. To indicate this only slight dissociation of carbonic acid, a dot replaces the straight line between its component ions.

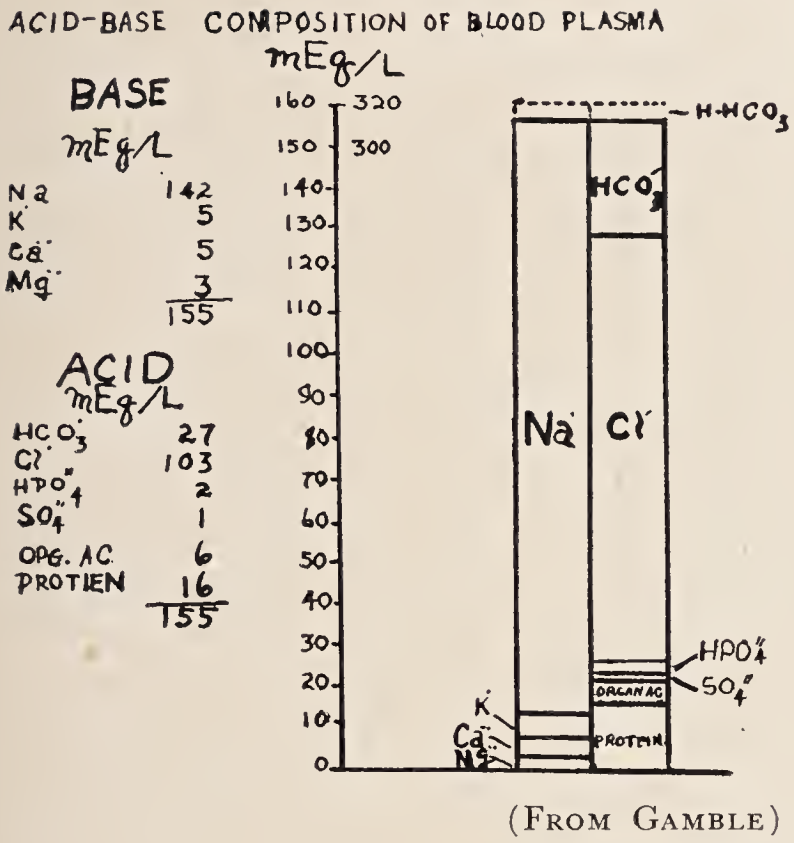
TABLE 3

WATER EXCHANGE PER DAY IN NORMAL INDIVIDUALS.



(FROM GAMBLE)

TABLE 4



(FROM GAMBLE)

OUTLINE OF UNITS OF MEASUREMENT.

mEq/liter (milliequivalents per liter) = $\frac{\text{mgm per liter}}{\text{equivalent weight}}$

equivalent weight = $\frac{\text{atomic weight}}{\text{valence of element}}$

mM/liter (millimols per liter) = $\frac{\text{mgm/liter}}{\text{molecular weight}}$

vol % (volume per cent) = mM/liter × 2.24 for a gas whose properties approach that of an ideal gas, such as oxygen of nitrogen; for carbon dioxide the factor is 2.226.

NORMAL BIOCHEMICAL VALUES

normal pH of the blood—7.35 to 7.45
normal pH of the urine—4.6 to 8.0 (usually around 6.0)
carbon dioxide content (CO_2 combining power)
serum 45–70 vol % (20–30 mM/liter)
blood 40–60 vol % (18–27 mM/liter)

((The carbon dioxide measured is the total amount of carbon dioxide (both as $H:HCO_3$ and $NaHCO_3$) in the blood or serum. The determination is usually performed by extracting carbon dioxide in a vacuum in the presence of lactic acid—van Slyke method)).

ACIDOSIS (pH DECREASED)

a) *Metabolic acidosis* is due to the accumulation of acid metabolites or to the ingestion of acids or to the loss of base. The carbon dioxide combining power is decreased. This state can occur in diabetes, diarrhea, and nephritis, etc. The great bulk of pediatric patients with an acid base imbalance belong in this group.

b) *Respiratory acidosis* is due to the inability to breathe off carbon dioxide. The carbon dioxide combining power is within normal limits or is increased. This state can occur in asthma and bronchiolitis, etc.

ALKALOSIS (pH INCREASED)

a) *Metabolic alkalosis* is due to the accumulation of base or to the ingestion of base or to the loss of acid. The carbon dioxide combining power is increased. This state can occur in vomiting, etc.

b) *Respiratory alkalosis* is due to the increased breathing off of carbon dioxide. The carbon dioxide combining power is within normal limits or is decreased. This state can occur in hyper-ventilation where tetany may result. In salicylate poisoning a respiratory alkalosis first occurs and, then, due to the accumulation of acid metabolites, a metabolic acidosis ensues within a few hours.

An acidosis or alkalosis can be compensated or uncompensated. In the former condition, the buffer system shifts with no abnormal change in the pH. In the latter state an abnormal change in the pH occurs. The lungs, by regulating the carbon dioxide exchange, are the first line of defence in this buffer system. The kidneys, by regulating the pH of the urine and by substituting

ammonia to conserve the other cations of the body, are the second line of defence.

As indicated above the determination of whether acidosis or alkalosis is present, cannot be made from the carbon dioxide combining power. Usually the clinical picture will indicate which of the two conditions is present. A pH determination[1] and a carbon dioxide combining power estimation are valuable. At the Hospital for Sick Children, much greater emphasis is placed on the pH determination than on the carbon dioxide combining power estimation in the evaluation of the severity of the condition, since, in an appreciable group of cases, the compensatory mechanisms, of which the carbon dioxide combining power is a measure, are not adequate. For example, a carbon dioxide combining power of 38.1 vol per cent and a pH of 7.05 were the determinations on a member of this group. Since the compensatory mechanisms were not adequate, the carbon dioxide combining power indicated a less serious condition than that which actually existed. Usually the carbon dioxide combining power is a valuable determination but an awareness of its limitations is important.

No specific symptomatology for acidosis or alkalosis exists. The symptoms depend on the mechanism. Usually dehydration—the symptoms of which are dry skin and mucous membranes, poor skin turgor, and sunken eyes—is present in both conditions. Shock, as evidenced by limpness and greyish colour of the skin, may be present. In the metabolic acidosis of diabetes, ketosis and hyperventilation are present. In the metabolic alkalosis of vomiting, tetany may be present. With overdosage of sodium bicarbonate, edema along with tetany may be present.

The great bulk of pediatric patients with acid-base inbalances belong in the metabolic acidosis group.

REPLACEMENT OF FLUID AND ELECTROLYTES

The features of parenteral fluid replacement will be discussed under the following headings: amount, electrolytes, calories, foodstuffs, vitamins, and drugs.

a) AMOUNT OF FLUID.—The amount of fluid to be given is a matter of clinical judgment and experience. Table 2 is helpful as a rough guide. As much as three to four ounces per pound per day is not an unusual requirement for an infant with diarrhea. It must be emphasized, however, that too much fluid may also cause severe damage.

b) ELECTROLYTES.—The proper electrolytes must be given to restore the acid base balance. In extreme shifts in the balance, the acid base regulating mechanisms of the body fail to function properly. Unless the balance is restored towards normal by parenteral fluid therapy within a short period of time, the compensatory mechanisms of the body cannot function adequately and, generally, death supervenes within a short period.

The proper amount of saline must be given in the fluid. Marriott emphasized the point that a pure deficiency of sodium chloride within the body is an entirely different entity than is a pure deficiency of water. Usually these two deficiency states are associated in children but occasionally a pure deficiency of

[1]As performed at the Hospital for Sick Children, the pH determination is sufficiently reliable for clinical purposes.

either one or the other is observed. An excess of saline in the parenteral fluid will produce edema although the patient may still be insufficiently hydrated.

In some cases, appreciable amounts of potassium and calcium may be required in the parenteral fluid.

The indications for and the amount of saline, potassium, and calcium to be given are a matter of clinical judgment and experience.

(Table 5 indicates the basal requirements of sodium chloride.)

TABLE 5

APPROXIMATE NORMAL SODIUM CHLORIDE MAINTENANCE ALLOWANCES PER DAY FOR RESTING NON-SWEATING PERSONS OF VARYING SIZE

Size	*Sodium Chloride*	*Physiological Saline Solution*
Infants	1 Gm.	125 cc.
Children	3 Gm.	350 cc.
Adolescents and adults	6 Gm.	700 cc.

(FROM BUTLER AND TALBOT)

Determinations of the sodium, potassium, calcium, and chloride in the blood are valuable but are tedious and expensive and should only be performed when indicated. Normal values at the Hospital for Sick Children are:

serum sodium	135–145 mEq per liter.
serum potassium	4.0–5.5 mEq per liter.
serum chloride	98–108 mEq per liter.
serum calcium	5.0–6.0 mEq per liter (9.0–11.5 mgm. per cent).

The Fantus Test (a simple quantitative test for the determination of urinary sodium chloride) is not of much value in infants because of the difficulty in collecting more than one or two urine specimens during the day.

c) CALORIES.—Although the provision of calories is not as immediate a consideration as the provision of sufficient fluid and the proper electrolytes, it is nonetheless a feature of parenteral fluid therapy.

Table 6 indicates the basal requirements of calories.

TABLE 6

APPROXIMATE DAILY CALORIC REQUIREMENTS OF NORMAL RESTING PERSONS OF VARYING SIZE

Size	*Daily Caloric Requirement* Cal./kg.
Young infants	60
Old infants	55
Children	30
Adolescents and adults	25

(FROM BUTLER AND TALBOT)

Glucose preparations are the most common source of calories. One hundred cubic centimetres of a 5% glucose solution provides 20 calories.

d) FOODSTUFFS.—Two of the three basic foodstuffs, carbohydrate and protein, can be easily provided in the parenteral fluid but solutions containing fat are not yet generally available. Glucose solutions, aside from providing calories, combat ketosis. Amigen, a protein hydrolysate, provides amino acids for tissue repair and is given to cover nitrogen loss. This solution is usually indicated only when prolonged parenteral fluid therapy is required. Serum protein values may be helpful in determining when amigen is indicated.

e) VITAMINS.—All the vitamins are indicated with prolonged parenteral fluid therapy.

f) DRUGS.—Most drugs are effective when given parenterally. Much discussion has ensued as to how to administer the sulfa drugs. The predominating current belief is that sufficient fluid administration is essential and that alkalinization is unnecessary.

ROUTES OF ADMINISTRATION

a) SUBCUTANEOUS: Subcutaneous replacement is the least difficult method of fluid and electrolyte replacement. This method is almost entirely confined to infants but can sometimes be used in older children when intravenous therapy is difficult to accomplish.

Two methods of replacement are available:

(i) continuous drip.
(ii) injection.

(i) CONTINUOUS DRIP.—This method is widely used. "Y" tubing with the needles inserted into the lateral aspect of the thighs, is the most common method of administration. As long as precautions against infection are observed, the needles may usually be allowed to remain in the same site for as long as two days.

A disadvantage of subcutaneous fluid replacement is that the body only relatively slowly draws upon this subcutaneous fluid which collects at the site of introduction into the body. This slow availability of this depot of subcutaneous fluid precludes its use in acute severe dehydration.

Recently hyaluronadase, a mucolytic enzyme, has been added to the fluid in order to hasten the absorption of this depot of subcutaneous fluid by the body. In the U.S.A. some workers are reporting that fluid administration with hyaluronadase is almost as equally effective in the treatment of severe dehydration and electrolyte inbalance as intravenous administration of fluid. Investigation of the use of hyaluronadase in subcutaneous fluid administration now being performed at the Hospital for Sick Children has so far failed to corroborate these claims although it does indicate that hyaluronadase does improve the effectiveness of subcutaneous fluid administration. Final conclusions about the effectiveness of hyaluronadase in parenteral fluid therapy have not as yet been made.

The sulfonilamide drugs can be given in this hyaluronadase subcutaneous solution.

(ii) INJECTION.—This method is used when administering 100 cc. or less of subcutaneous fluids. In some centres it is the usual method in the newborn period. The fluid is injected subcutaneously by means of a large syringe and long needle into any of the areas of the body which are suitable for this method of administration. In order of relative frequency of use, these areas are the back, the front of the chest or abdomen, the axilla, and the thighs. The use of an area of the body which will be detrimental to the condition of the patient is contraindicated. For example, in patients with pneumonia the use of the chest for the subcutaneous accumulation of fluid is avoided.

At the Hospital for Sick Children, the injection of subcutaneous fluid is avoided because of the increased trauma and risk of infection. A modification of the continuous drip method is used during the newborn period. The fluid is allowed to drip as quickly as possible under the skin of the anterior chest wall by means of the "Y" tubing apparatus. This procedure is performed as frequently as three times a day and usually requires on each occasion only about twenty minutes because of the small amount of fluid involved.

b) INTRAVENOUS: Intravenous replacement is the route of choice because this method most rapidly and effectively combats fluid and electrolyte inbalance.

The disadvantage of intravenous replacement is that in infants this route of administration is not infrequently difficult.

Two methods of replacement are available:

(i) continuous drip.

(ii) injection.

(i) CONTINUOUS DRIP.—This method is almost exclusively used in children over 2 years and, in all but the younger age group, can usually be performed quickly and with little difficulty. As with adults, the veins in the cubital fossa or on the dorsum of the hand or foot are commonly used. In infants intravenous replacement presents a more difficult problem. Frequently the only veins which are available are the veins in the scalp. Continuous fluid administration by means of a scalp vein is becoming increasingly popular at the Hospital for Sick Children. Intravenous replacement by means of a scalp or other vein in infants requires some skill and practice because of the small calibre of the vessels. Another popular method of continuous replacement is by means of a cut-down on the long saphenous or other accessible vein.

ii) INJECTION.—This method is less popular and obviously more dangerous than the continuous method. Occasionally, when a continuous intravenous cannot be performed or is not desired, blood or other parenteral fluid is injected usually by means of a scalp vein as rapidly as possible. A "two-way" stop cock is used in this "push" intravenous. Ten to fifteen cubic centimetres per pound of body weight is the maximum amount advised to be given at one time to an infant in good condition. For infants in poor condition, particularly when evidence of cardiac damage is present, a correspondingly smaller amount is advised.

c) INTRAMEDULLARY: This method of replacement is used in Sweden and Israel; and occasionally in the U.S.A. when a rapid method to correct fluid and electrolyte inbalance is required and the intravenous method is not available. The upper end of the tibia is the usual site for the injection or the continuous drip of the parenteral fluid. The chief objections to this method are the risk of infection and the difficulty. No occasion has arisen in the Hospital for Sick Children to use this method.

GAVAGE, although not a parenteral route, should not be ignored as a means of supplying fluid and necessary food substances to the patient. This procedure is particularly indicated and effective in prematures and unconscious patients.

SOLUTIONS AVAILABLE AND INDICATIONS FOR THEIR USE

The solutions listed below can be given intravenously or subcutaneously. If given subcutaneously, the solution must not be hypertonic.

a) NORMAL SALINE—9 gms. of sodium chloride in 1000 cc. of water.

b) RINGER'S LACTATE—

Ringer's:

8.6 gms. of sodium chloride .3 gms. of potassium chloride .33 gms. of calcium chloride	in 1,000 cc. of water.

Ringer's lactate (Hartmann's solution):

850 cc. of Ringer's 150 cc. of 1/6M sodium lactate	In 1000 cc. of water.

c) GLUCOSE.—Usually administered as a 5% solution which is almost isotonic; also administered intravenously as a 10% solution which is hypertonic.

The above three solutions are the

commonest parenteral solutions used in pediatrics. Frequently the glucose solution is combined with either the saline or the Ringer's lactate solutions. At the Hospital for Sick Children, a solution made up of 2 parts of 5% glucose and 1 part of saline is the commonest parenteral solution used. Usually in a dehydrated, mildly acidotic infant or child, this solution ("2/3 and 1/3") provides the requirement of saline, and sufficient glucose to combat ketosis when the proper amount of fluid is administered. Some clinicians at the Hospital for Sick Children are replacing the saline part with Ringer's lactate because of the two advantages that the Ringer's lactate possesses—the solution provides potassium and calcium ions; and, because of the lactate, is a mildly alkalinizing solution.

d) 1/6M SODIUM LACTATE.—This solution is an alkalinizing solution which is comparable to a 5% sodium bicarbonate solution. Sodium lactate is used in pediatrics instead of sodium bicarbonate because of its greater margin of safety. With the sodium lactate solutions, the sodium becomes available for the formation of bicarbonate when the lactate is oxidized. Since the lactate is usually metabolised slowly and as required, less chance of producing an alkalosis exists with this solution than with a sodium bicarbonate solution.

Roughly, in a metabolic acidosis, 1 cc. of a 1/6 M sodium lactate solution per pound of body weight raises the carbon dioxide combining power 1 vol. per cent.

When the carbon dioxide combining power is above 30 vol. per cent and the pH is within normal limits, the buffer system of the body will correct the condition without the aid of 1/6 M sodium lactate solution as long as sufficient saline, glucose, and fluid are provided.

When the carbon dioxide combining power is below 30 vol. per cent, and the pH is within normal limits, an amount of 1/6 M sodium lactate is suggested that will by calculation raise the carbon dioxide combining power to 35 vol. per cent. The buffer systems of the body will continue to correct the condition as long as sufficient saline, glucose, and fluid are provided.

When the pH is decreased, an amount of 1/6M sodium lactate is suggested that will by calculation raise the carbon dioxide combining power to within the normal range since the buffer system of the body may be temporarily inadequate.

Clinical judgment and experience are the most important factors in determining when and how much 1/6M sodium lactate is to be given. Before the results of the carbon dioxide combining power and the pH are available, the clinician estimates what he believes these values to be and prescribes the quantity and composition of the parenteral solutions accordingly. Later, possibly within a few hours, he may modify the parenteral solutions when these determinations are available. During the course of therapy he may check his clinical judgment with laboratory determinations of the carbon dioxide combining power, the pH, sodium, potassium, calcium, chloride, etc.

For severe alkalosis 1/6 M ammonium chloride has been suggested but at the Hospital for Sick Children alkalosis has always been treated effectively with 5% glucose in normal saline; and this solution has never been used. When as solution with normal saline is used, care should be taken to avoid administering an excess of saline.

c) DARROW'S SOLUTION.—This solution contains a relatively large quantity of potassium—nine times the amount in Ringer's solution.

Darrow's solution:

2.7 gms. of potassium chloride 3.0 gms. of sodium chloride 300 cc. of 1/6 M sodium lactate	In 1000 cc. of water.

Potassium deficiencies may occur in severe cases of diarrhea and diabetic coma. The symptoms which are not specific include muscle weakness, lethargy, intestinal distention, myocardial degenerative changes, edema of the lungs, and putty-like consistence of the muscles. In the presence of severe potassium deficiency the clinical condition of the child will rapidly deteriorate unless the deficiency is promptly corrected. Serum potassium levels below 3 mEq per liter indicate an unfavourable prognosis unless corrected.

Severe potassium deficiency states are rarely observed in pediatrics where most cases of dehydration are acute and of one to three days' duration. The early oral feeding of milk, broth, fruit juices, and/or Darrow's solution—all of which contain an appreciable amount of potassium—and the use of Ringer's lactate in the parenteral therapy, usually correct minor deficiencies.

When a severe potassium deficiency is suspected, a definite routine is suggested. Before Darrow's solution is administered, the patient must be adequately hydrated and the kidneys must be functioning properly as evidenced by a satisfactory urinary output. A serum potassium level should be obtained and should be below the normal limits. Electrocardiograph changes—such as a lowering and broadening of the T wave, a lengthening of the QT interval, and a depression of the ST segment—are possibly a more reliable indication of an intracellular potassium deficiency than is a decreased serum potassium level. Either a serum potassium level or an electrocardiograph reading (or preferably both) should be obtained before Darrow's solution is administered.

The amount of Darrow's solution suggested to correct the potassium deficiency is 25 cc. per pound per day. The solution if given intravenously should be diluted with glucose solution and given slowly—preferably over a period of eight hours. A check of the potassium level in the body by means of the serum levels or the cardiograph tracing (or both) should be performed after each daily administration. Death can occur with potassium serum levels of 10 mEq. per liter. The electrocardiograph changes due to hyperpotassemia are roughly the opposite to those of hypopotassemia. These changes are tall T waves with a narrow base, broad QRS's, and the disappearance of the P waves.

Generally when indicated, the one parenteral administration will produce a dramatic response in the patient's condition.

f) CALCIUM GLUCONATE.—Calcium gluconate is indicated in the recovery period of some cases of severe diarrhea where tetany may occur because of the loss of calcium in the stools. Calcium gluconate because of the possibility of sloughs is not given subcutaneously or intramuscularly—only intravenously.

g) AMIGEN.—Amigen 3 1/3%, dextrose 3 1/3%, in 1/3 Ringer's lactate solution, is recommended for subcutaneous use. Amigen 5% in 5% dextrose solution is recommended for intravenous use. Ingredients must not be added to the amigen solution and great care

in the administration must be exercised. The amount of amigen indicated depends chiefly upon the protein stores of the body.

h) BLOOD AND PLASMA.—Not more than 10 to 15 cc. of blood or plasma per pound of body weight is advised to be given by a "push" transfusion at any one time. Although usually this same figure is adhered to when giving blood or plasma by the continuous drip method, it can be exceeded with safety when the blood or plasma is given slowly to a patient who has no cardiac damage. Roughly 10 cc. of blood per pound of body weight will raise the hemoglobin 2.5 gms. per cent. The indications for the use of blood or plasma in infants and children are the same as those for adults.

CONCLUSION

Now that the complexities of parenteral fluid therapy in pediatrics have been discussed, emphasis on the most important point is necessary. About four-fifths of the patients admitted with dehydration and acid-base inbalance to the Hospital for Sick Children require for a prompt cure only "2/3 and 1/3" (3 1/3% glucose in 1/3 strength normal saline). No blood chemical determinations need be performed. For only 1/5 of the patients admitted with dehydration and acid-base inbalance is a knowledge of the complexities of parenteral fluid therapy essential.

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AMERICAN ACADEMY OF PEDIATRICS MEETS IN TORONTO

More than 2,000 specialists in the fields of children's physical, mental and emotional health are expected to meet in Toronto when the American Academy of Pediatrics holds its annual meeting at the Royal York and other hotels Oct. 22nd to 25th. The academy includes about 3,000 of the outstanding pediatricians in the United States, Canada, Cuba, Mexico and Central and South America.

All phases of children's health will be discussed in special seminars, round tables and panels and scientific papers concerning the latest developments and discoveries in diseases pertaining to infants will be read. The special seminars begin Oct. 19th, but the meeting proper will not start until Monday, Oct. 22nd. Although the meetings will not be open to the public, newspaper and magazine representatives will be allowed free access to the proceedings.

DIAGNOSIS OF SOME COMMON ACUTE ABDOMINAL CONDITIONS

G. J. HALPERN, 5T2

SIX CONDITIONS COMMONLY MISDIAGNOSED

According to Thorek, there are "six outstanding conditions" presenting a picture of an acute abdomen which are misdiagnosed more frequently than any of the numerous others. Strange though it may seem, these conditions are among the most common giving abdominal pain. They accounted for approximately 45% of 200 cases of acute abdominal pain, examined in a recent analysis by Macdonald. Each of these six diseases has characteristic features which, in many instances, will make the diagnosis obvious to the medical practitioner who is thoroughly familiar with them. If a mistaken diagnosis turns out later to involve one of the relatively uncommon abdominal conditions, not included in this group, the error will at least be more palatable than a misdiagnosis of a common condition with conspicuous signs and symptoms. The conditions most frequently misdiagnosed are as follows:

1. Acute appendicitis.
2. Acute (obstructive) cholecystitis.
3. Perforated peptic ulcer.
4. Acute hemorrhagic pancreatitis.
5. Renal colic.
6. Acute coronary occlusion.

A summary of the main features of these conditions, emphasizing the characteristic clinical manifestations essential to diagnosis, is presented:

1. Acute Appendicitis

INCIDENCE: This condition may occur at any age, but is most frequently seen in adolescents and young adults; more common in males.

HISTORY: There is often a history of indigestion or flatulence for several days prior to the onset of the attack. Commonly, loss of appetite, nausea and vomiting occur, but these tend to be absent in the adult. Constipation occurs more frequently than diarrhoea, but the latter is often seen in children. Onset of pain is acute, though at first not marked; it starts in the epigastric or umbilical region. Later, there is an increase in the severity of the pain, and cramp-like paroxysms are characteristic. The pain then changes, becomes sharp or cutting in character, and localizes in the right iliac fossa, the exact site depending on which of the nine positions the appendix is to be found.

CLINICAL PICTURE: Pain, localized tenderness and muscle spasm over the site of the appendix are the most reliable symptoms and signs. Rebound tenderness occasionally is present without deep tenderness being elicited. Distension and superficial hyperaesthesia are inconstant findings. There is tenderness at McBurney's point only when the appendix happens to lie beneath it. Local deep tenderness is a constant finding when the appendix is outside the pelvis. Rarely there is testicular pain; rarer still, chills. As a rule there is lowgrade fever. If the rectal temperature within 24 hours of onset is 103° or over, it is probably not acute appendicitis. The pulse is not diagnostic; it increases 10 beats per minute for every 1° F. rise in temperature. However, a

pulse over 110, and rising, in cases of appendicitis suggests that perforation may have occurred.

SOME AIDS TO DIAGNOSIS

Laboratory: A white blood count of 10,000 to 20,000 is confirmatory evidence of acute appendicitis in the presence of the classical symptoms and signs. The leucocyte count may, however, be normal.

"Two-Question Test": 1. "Where was your pain when it started?" 2. Where is your pain now?" (See above).

Iliopsoas Sign: Patient is placed on left side and right leg is hyperextended. If positive, pain is elicited in the right lower quadrant. This signifies that the inflamed appendix is overlying the iliopsoas and is retrocecal.

Obturator Sign: With patient on his back the right thigh is flexed upon the abdomen and the leg upon the thigh; the leg is then abducted. This stretches the obturator internus muscle, and if pain is produced is diagnostic of a fascitis involving the obturator fascia. This finding, together with a history of acute appendicitis, may give the diagnosis and tell us that the appendix is low-lying and in the pelvis.

2. ACUTE (OBSTRUCTIVE) CHOLECYSTITIS

INCIDENCE: According to Thorek, this disease is commonly seen in a patient described by the "7 F's"; viz., "fair, fat, fertile, flatulent, flabby female of forty." But this condition may occur in thin males of any age.

HISTORY: As this condition is usually a complication of cholelithiasis (formation of stones in the gall-bladder), a history of previous attacks aids in the diagnosis. The sharp pain is associated with the sudden passage of a stone down the cystic duct or its impaction in the neck of the gall-bladder. Instead of passing off within a short time, the colic changes to acute stabbing epigastric agony, which becames localized in the right subcostal region.

CLINICAL PICTURE: Severe, stabbing pain, localized under the right costal margin or referred to the region overlying the stomach, is the main feature. The classical picture is one where the pain radiates from the right costal margin along the path of the seventh intercostal nerve to the inferior angle of the right scapula. Gall-bladder pain does not radiate to the right shoulder. When a gall-bladder patient has shoulder pain a diagnosis of gangrenous or ruptured gall-bladder with biliary peritonitis should be considered.

There is usually marked rigidity of the right rectus muscle.

Vomiting and constipation are almost constant accompaniments. The temperature is usually below 102°. Pulse is not of diagnostic value.

A palpable mass in the right upper quadrant is present in about 20% of cases.

Jaundice is present only rarely, but when this is the case, rules out acute abdominal conditions not associated with the biliary tract.

SOME AIDS TO DIAGNOSIS

Check for jaundiced sclera.

Two Questions: 1. "Where is the pain?" 2. "Where does it go to?" (See above).

Murphy's Sign: Place the left hand on the costal margin in such a manner that the thumb lies over the fundus of

the gall-bladder. The thumb exerts moderate pressure. Ask the patient to take a deep breath. The sign is positive if the patient "catches her breath" when the descending diaphragm causes the inflamed gall-bladder to impinge against the pressure of the thumb.

Boas' Sign: Test for an area of hyperesthesia on the right side posteriorly from 1″ lateral to the spines of the vertebrae to the posterior axillary line, and vertically between the levels of the 11th thoracic to 1st lumber spines.

X-Ray (Flat-plate) may on rare occasion reveal the presence of stones in the gall-bladder or ducts.

3. Perforated Peptic Ulcer

INCIDENCE: This condition is rare in females.

HISTORY: Usually the patient has a previous history of peptic ulcer, rarely with haemorrhage; however, the onset may be with perforation. This abdominal catastrophe usually occurs with dramatic suddenness, following eating. The pain is often so severe that it causes the patient to double up and leaves him in a state of shock couplied with board-like rigidity of the abdominal wall.

CLINICAL PICTURE: According to Cope there are three stages in the process following perforation:

(1) Stage of Primary Shock:
Characterized by:
- Severe and generalized abdominal pain.
- Anxious countenance; livid or ashen appearance.
- Cold sweating face, and cold extremities.
- Subnormal temperature (95 or 96° F.).
- Shallow respiration.
- Retching or vomiting.
- Pain on the top of one or both shoulders.
- Pulse rate is usually normal during the first six hours—a point not commonly appreciated.

(2) Stage of Masked Peritonitis:
Characterized by:
- Cessation of vomiting.
- Reduction of abdominal pain.
- Improvement of general appearance; face regains normal colour.
- Temperature returns to normal.

Thus, the general symptoms temporarily improve, but all the local signs remain and become still more definite:
- Abdominal wall very rigid, tender and often retracted or flat.
- Peritoneum tender on rectal examination.
- Great pain on movement of body.
- Presence of pneumoperitoneum (Air in the peritoneal cavity is demonstrated by percussion: there is a diminution or absence of liver dullness.)

(3) Stage of Frank Peritonitis:
A discussion of peritonitis is presented farther on in this paper. Early operation will prevent this stage from being reached.

AIDS TO DIAGNOSIS

X-Ray—Sometimes quantities of free gas are seen between the liver and diaphragm.

PERFORATION OF PEPTIC ULCER SIMULATING APPENDICITIS

At times the duodenal contents from a perforated ulcer gravitate along the

outer side of the colon and collect in the right iliac fossa. Several hours after perforation, tenderness and muscle spasm may be found over the appendix. An accurate history and X-Ray studies usually indicate the correct diagnosis. On laparotomy a healthy-looking appendix, coupled with turbid fluid in the peritoneal cavity, should automatically direct the surgeon's attention to the stomach and duodenum.

Another point: Test knee-jerk and reaction of the pupils to light, to rule out gastric crisis of tabes. Board-like rigidity, the cardinal sign of perforated ulcer, does not occur in tabetic crises.

4. Acute Hemorrhagic Pancreatitis

INCIDENCE: Commoner in stout individuals over forty; particularly females.

HISTORY: Frequently, there is a history of gall-bladder disease. Dramatically sudden in onset and usually after a heavy meal or alcoholic bout, severe epigastric pain which radiates to the left of the midline, around the body or through to the back, and on occasion to the shoulders, is followed by a shock-like state.

CLINICAL PICTURE

Pain: Relieved when patient sits up or lies on his abdomen, but is aggravated when he is on his back.

Shock: In severe cases, profound shock usually accompanies the pain; cold and clammy extremities, subnormal temperature, and a rapid, thready pulse. Cyanosis is usually seen and dyspnoea occasionally noticeable.

G.I. Signs: Localized epigastric tenderness and rigidity between the umbilicus and the xiphoid. Reflex vomiting or retching nearly always occurs. Abdominal auscultation reveals a quiet but not silent abdomen. A mass or tenderness is frequently found in the left upper quadrant. Mild jaundice is present in about 50% of cases.

Extravasated Blood: An uncommon finding is ecchymosis in one or both loins, or at times around the umbilicus.

AIDS TO DIAGNOSIS

Serum Amylase—an increase is highly suggestive of this condition.

White Blood Count—is usually quite elevated.

Urinalysis—a marked glycosuria is sometimes observed.

5. Renal Colic

INCIDENCE: More common in males.

HISTORY: Patient often reveals a history of previous attacks, rarely a hereditary influence, very rarely a story of gout or parathyroid disease. The present attack is sudden in onset.

CLINICAL PICTURE: The classical picture of pain starting in the lumbar region and radiating to the testicle, vulva or inner aspect of the thigh, is seen when a small renal stone is impacted in the lower third of the ureter or at the ureteropelvic junction. If the stone is large and is lodged in the renal pelvis, the pain is dull and is felt in the loin; colic in these cases is rare. Tenderness may be present in the costovertebral region or, with ureteral colic, along the course of the ureter. Secondary hydronephrosis may make the kidney palpable. The patient is usually extremely restless compared to the perfect quiet of the patient with peritonitis. Vomiting is a common symptom. There is frequency of urina-

tion and during the act of micturition the pain may be altered. Bradycardia is often seen; a patient with acute abdominal pain who has a slow pulse and a clean tongue suggests renal colic as a likely diagnosis.

AIDS TO DIAGNOSIS

A flat X-Ray film may reveal the presence of a stone in the pelvis or ureter.

Intravenous and retrograde pyelography make it possible to detect stones in about 95% of cases. An intravenous pyelogram of the kidney on the affected side usually shows increased density, since the dye in the renal tubules is more concentrated; relative or complete anuria is seen on the affected side.

A catheter specimen of urine may reveal pus, blood and albumin.

6. Acute Coronary Occlusion ("Heart Attack")

INCIDENCE: More common in patients over 40; especially males in the professions or having sedentary occupations.

HISTORY: Although the "heart attack" often comes like a bolt out of the blue, there is usually a history of shortness of breath or pain in the chest during exertion or excitement. On occasion there is a history of previous "heart attacks" or of long-standing epigastric pain and tenderness over an enlarged, congested liver.

CLINICAL PICTURE: The patient is pale, with lips white, and often gives the impression of extreme fright. He sweats profusely. He describes the substernal pain as a crushing pressure which prevents him from breathing properly. He is usually restless, compared to the quiet of the patient with a perforated peptic ulcer, the condition with which certain cases of "heart attack" are most likely to be confused. The pain, itself, may be similar in distribution to that of angina pectoris, but is not relieved by nitrites and may require repeated doses of morphine to be subdued. Signs of impaired circulation are often present, such as dyspnoea, orthopnoea and cyanosis. The blood pressure is usually low, and there is a rapid, feeble pulse. Other findings sometimes seen are cardiac enlargement, feeble heart sounds, tachycardia and arrhythmia. Very rarely a pericardial friction rub may be heard several hours after the attack, and this is confirmatory evidence of myocardial infarction. Auscultation at times reveals crepitous râles in both bases due to pulmonary congestion. A cough may develop on the second day, and may or may not be productive of sputum.

Auscultation of the abdomen will reveal normal intestinal sounds, which are absent or diminished in cases of peritonitis. Gastrointestinal symptoms such as epigastric pain, nausea, vomiting and constipation are often present, but should not confuse the issue in the face of the cardiopulmonary signs and symptoms, and in the absence of any change in liver dullness and signs of peritoneal irritation.

AIDS TO DIAGNOSIS

Electrocardiogram—presents in majority of cases a pathognomonic picture, but should be taken at least 24 hours after the attack.

Leukocytosis and increased Sedimentation Rate accompany the characteristic fever and usually appear after 24 to 48 hours.

A SEVENTH CONDITION— ACUTE INTESTINAL OBSTRUCTION

This condition occurs with sufficient frequency to warrant special attention. It usually results from one of the following:

(a) Strangulation of a loop in a hernial sac or beneath bands of acquired or congenital adhesions.
(b) Twisting of part of a loop on itself (volvulus).
(c) Telescoping of intestine into itself (intussusception).
(d) Blocking of the lumen by tumour, foreign body, or fecal mass.
(e) Contraction of an annular neoplasm or of inflammatory tissue surrounding the wall.
(f) Pressure from without, as by tumour of some other abdominal structure.

INCIDENCE: No special age or sex incidence.

HISTORY: Sudden onset of pain and vomiting. There may be a history of hernia of long standing, or of a previous abdominal operation. There is a gradual onset of shock, a few hours in the case of high obstruction or a day or two in the case of low intestinal obstruction.

CLINICAL PICTURE: Usually, the higher the point of obstruction, the more rapidly do symptoms develop.

Pain is the first symptom. In the early stages, while peristalsis is active, the pain may be colicky or cramp-like, later becoming a steady ache with occasional spasmodic exacerbations as the intestine distends and peristalsis diminishes. If the obstruction is in the small bowel or ileocecal region, the pain is usually at or above the umbilicus. If it is in the large bowel, pain is felt below the umbilicus, rarely above it.

Vomiting is usual, frequent and copious. In small bowel obstruction it begins immediately, while in large bowel obstruction it is a late manifestation, or may not occur at all.

Distention may be confined to the epigastrium if the obstruction is high, but if the lower part of the ileum is obstructed, the abdomen is symmetrically distended, and the characteristic ladder pattern may on rare occasion be seen.

Shortly after the onset of obstruction the bowel distal to the lesion may empty itself by one or two movements. There is, other than this, no passage of fecal material or even gas.

In early stages of obstruction, auscultation will reveal the loud, high-pitched noises of active peristalsis which may or may not be palpable or visible. In the later stages, peristaltic waves and sounds become infrequent or disappear entirely.

A mass may be visible or palpable. This may consist of a loop of distended intestine, a mass of inflamed tissue, or actual tumour.

Slight general tenderness is usually present. The abdominal wall is tense, but true muscle spasm is not, as a rule, seen.

In children, particularly those under 2 years of age, pallor, periodic attacks of pain, vomiting, passage of mucus and blood per rectum ("red-currant jelly" stool) and the presence of a palpable abdominal tumour means intussusception. In patients of the older age group (i.e. those over 50) neoplastic ulceration with erosion and possibly perforation, should always be borne in mind as a possibility. The most common cause of acute obstruction is strangulated external hernia.

Whenever there is a lack of local physical findings in a patient with intense abdominal pain, nausea and vomiting, a diagnosis of intestinal obstruction must be considered.

SOME POINTS IN DIAGNOSIS

The hernial sites should first be examined: inguinal, femoral and umbilical.

On auscultation, listen for borborygmi at the height of the intermittent pain. (Borborygmi are gurgling, bubbling sounds much like those produced by pouring water out of an inverted bottle with a narrow neck.) Unless the noises are due to intestinal colic, as a rule there is no intimate time relationship between pain and borborygmi.

DIFFERENTIAL DIAGNOSIS

It is important to remember that there is a formidable array of conditions which on occasion must enter the differential diagnosis of an acute abdomen. The more common of these are as follows:

IN WOMEN:

Ruptured graffian follicle ("Mittelschmerz").
Acute salpingitis.
Ruptured ectopic pregnancy.

IN BOTH SEXES:

Mesenteric lymphadenitis.
Mesenteric thrombosis or embolism.
Ulcerative colitis.
Regional ileitis.
Perforated diverticulum.
Perforated carcinoma of the large bowel.
Ileo-caecal tuberculosis.
Torsion of the omentum.

PORPHYRIA

In recent years an interesting but fortunately rare condition known as porphyria has been added to the list of diseases capable of simulating an acute abdominal state. As surgery is contraindicated in this condition, porphyria must enter the differential diagnosis in all cases of severe abdominal pain where the symptomatology is atypical, particularly in patients who are hysterical or who have an obscure neurological disturbance, for example an unexplained peripheral neuritis. In this "inborn error" of porphyrin metabolism, the urine turns dark on exposure to sunlight, and hence the problem of diagnosis is not insurmountable if one remembers to watch out for porphyria.

COMPLICATION: ACUTE PERITONITIS

Acute inflammation of the peritoneum is the result of bacterial infection and may be either primary or secondary. Primary peritonitis (streptococcal or pneumococcal) occurs chiefly in infants and children, and apparently is a blood-borne infection frequently preceded by an upper respiratory disease. Most commonly, however, it is a sequel to perforation of an inflamed appendix, peptic ulcer, gangrenous gall-bladder, or rupture of a liver or kidney abscess. Occasionally a gonococcal salpingitis, or other genital tract infection in women, precedes a fatal peritonitis. Gangrene of any strangulated, or otherwise ischaemic coil of gut inevitably leads to peritonitis.

According to Cope, two classes of symptoms present themselves: (a) those due to reflex action; and (b) those due to absorption of toxins.

(a) DUE TO REFLEX ACTION

Pain — Vomiting — Hiccuping — Rigidity of Abdominal Muscles—Superficial Hyperesthesia.

Pain is the most constant symptom. If the peritonitis is focal, the pain is usually localized; if the inflammation is extensive, the pain will be general. It is continuous and generally cutting or burning in character, but fluctuates in intensity, and is marked by bouts of colic. Hiccuping may be persistent. The face is flushed, there is a furred tongue, and usually constipation. Tenderness is a constant feature over any focus of peritoneal inflammation, and is increased on deep pressure. Rebound tenderness is present even when rigidity of the abdominal wall is absent. In pelvic peritonitis tenderness may be elicited only by rectal or vaginal palpation. Nausea and vomiting is common at the onset of peritonitis; the later vomiting is usually due to obstruction. Rigidity of the abdominal muscles is usually limited to the region of the lesion. If severe, it may cause the patient to lie with his knees drawn up to relieve tension on the affected muscles. It is in peritonitis following perforation of a peptic ulcer that rigidity of the abdominal musculature is most marked, due to the considerable peritoneal involvement. Cutaneous hyperesthesia is frequently present in the region below the umbilicus, particularly on the right side. Often it is limited to a narrow strip above both inguinal ligaments.

(b) DUE TO THE TOXEMIA

Distension—Diminution or Absence of Peristaltic Activity—General Toxemia and Collapse.

The toxic symptoms of peritonitis appear in the later stages and indicate that the infective agent is spreading throughout the vast surface area of the peritoneum. An occasional intermittence of the pulse is an indication of advancing peritonitis. As the infection involves the coils of intestine they become paralyzed, with resultant stagnation and obstruction. Distention and tympany may become extreme. The absence of peristaltic activity, as determined by auscultation, is perhaps the most important sign of general peritonitis. Boyd states that the great danger at this time is paralytic ileus rather than the toxemia.

The systemic reaction to the infection is a high fever, a rapid, weak pulse, and vomiting. Respiration is elevated, but not laboured. The leukocyte count is usually quite high. The patient is alert and apprehensive; his mind remains clear until the end is near.

The Hippocratic facies present in peritonitis is simply a picture of extreme collapse: the face is white and haggard-looking, nose is sharp, temples sunken, and ears are cold. It is not so much a sign of peritonitis as the mask of death following peritonitis.

In conclusion, the occurrence of severe abdominal pain of sudden onset in a patient who was previously well, is perhaps the most common emergency seen in medical practice. More often than not surgical intervention is indicated if the pain lasts more than six hours. Early diagnosis is, therefore, of the utmost importance.

ACKNOWLEDGEMENT

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PROPER NAMES QUIZ

It has long been a custom in Medicine to affix to various pathological conditions the name, or names, of those physicians who concerned themselves with the lesions. This practice is becoming less common, and gradually both textbooks and teachers are abandoning these proper names and falling back on anatomical and pathological descriptive terms. Still, the ability to pull a name like "Pellegrini-Stieda's Disease" out of the hat when confronted by a patient with an ossified medial collateral ligament of the knee brings a pleasant glow of satisfaction to the student, and expressions of wonder and amazement to the faces of his contemporaries (and clinician).

Here then are twenty proper names. Can you identify the pathological conditions that they represent?

1. Albers-Schonberg disease
2. Buerger's disease
3. Addison's disease
4. Banti's disease
5. Crohn's disease
6. Cushing's disease
7. Economo's disease
8. Hansen's disease
9. Hirshprung's disease
10. Kummell's disease
11. Legg-Perthes disease
12. Little's disease
13. Lorain syndrome
14. Parkinson's disease
15. Pott's disease
16. von Recklinghausen's disease
17. Simmond's disease
18. Tay-Sachs disease
19. Werlhof's disease
20. Weil's disease

(***Answers on Page 36***)

HEPARIN AND ITS RELATION TO THE NORMAL STABILITY OF CIRCULATING BLOOD AND PATHOLOGICAL HEMORRHAGIC CONDITIONS

F. C. MONKHOUSE*

The story of the discovery and development of heparin is widely known, and excellent reviews (6), (22) are available in the literature on the properties and uses of this powerful anticoagulant. There can be little doubt of its importance in the field of medicine and surgery. Much of the vascular surgery now carried out with the aid of heparin was considered impracticable before the material was available for clinical use. And, while there is still much debate concerning the best way to administer heparin as a therapeutic agent for relief or prevention of thrombotic conditions, (23), (24), (10) its value, in at least some of these cases, is not seriously questioned.

On the other hand, the importance of heparin in maintaining normal blood fluidity or as a contributing cause of hemorrhage in pathological conditions has not been established. While heparin has so far never been extracted from normal blood, or definitely shown to exist therein by any indirect method, it seems to be fairly generally accepted as a normal constituent of blood. Furthermore, in recent years articles have been appearing in increasing numbers attributing the hemorrhage associated with a variety of abnormal conditions (4), (5), (1), (20) to an increased level of blood heparin. What are the justifications for these views? Let us first consider the question of normal blood heparin.

HEPARIN AND NORMAL BLOOD STABILITY

The question as to why blood remains fluid in the normal healthy vessels and yet coagulates rapidly at the site of injury, or when placed in a foreign vessel, appears to have interested medical men for centuries. William Hewson (15) was probably the first to carry out investigations using the vessels of living animals. John Hunter, (19) a contemporary of Hewson, carried out many ingenious experiments on blood clotting, both *in vitro* and *in vivo*, and appears to be among the first to suggest that blood itself contained some factor which normally kept it fluid. Alexander Schmidt in 1892 (32) maintained that normal blood contained an inhibitor to coagulation and Morowitz (28) demonstrated the presence of a substance in serum and plasma which was specifically inhibitory to thrombin. Thus by 1905 the two phase "classical theory" of blood clotting was established.
(e.g.)

$$\text{Prothrombin} + \text{Ca} + \text{Thromboplastin} \rightarrow \text{Thrombin}$$

$$\text{Thrombin} + \text{Fibrinogen} \rightarrow \text{Fibrin.}$$

The fluidity of blood within the vessels was attributed to lack of thromboplastin and the presence of antithrombin, with the former being the most important. Howell, (16) showed that simple dilution would cause cell-free plasma to

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clot in paraffined vessels, and to explain this suggested that normal circulating blood contained all the factors necessary for coagulation, namely, calcium ions, prothrombin and fibrinogen. They were prevented from reacting, however, by the fact that antithrombin was also present and this substance prevented the calcium from activating the prothrombin to thrombin. When blood was shed the restraining effect of the antithrombin was neutralized by the action of thromboplastin furnished by platelets and tissues. When McLean (25) working in his laboratory discovered a powerful anticoagulant in dog liver extract, Howell concluded that this substance must be the natural anticoagulant responsible for the stability of prothrombin. In order to substantiate his theory it was necessary to establish that blood normally contained heparin. Methods for purification of heparin at that time were crude and he appears to have attempted the isolation only from dog's blood. (17) From the total blood of a dog he prepared a precipitate which when extracted with saline showed weak anticoagulant and antithrombic potency. In view of present knowledge concerning blood clotting and anticoagulants, such a result would not be considered conclusive. Nevertheless, because the method used was identical with that employed in extracting heparin from dog liver and an anticoagulant from peptone blood, Howell considered his results sufficient justification for his theory that heparin was a normal constituent of blood. Since that time, as more of the physical and chemical properties of heparin have been discovered, renewed attempts have been made to establish a normal heparin level. But all we have succeeded in doing so far is to show that it must be less than a certain amount, and as the sensitivity of our extraction methods has increased this figure has diminished.

Results of Direct Extraction

Charles and Scott (7) extracted 60 mg. of a weak anticoagulant material from a liter of ox plasma, and Wilander (35) suggested an upper limit of 1½ mg. per liter of plasma. Best, (6) summarizing the work up to 1940, suggested that the question of heparin in normal blood was still an open one, but that on the basis of the work of his group it must be less than 0.1 units per ml. of blood.

In 1949 Jaques, Monkhouse and Stewart (21) reported the development of a method capable of recovering small amounts of added heparin quantitatively from blood. With this method an attempt was made to establish a heparin level in normal human blood. In an experiment carried out on 22 healthy medical students, using 20 ml. of blood from each subject, precipitates were obtained which gave weak antithrombic titrations averaging the equivalent of 0.01 units per ml. of blood when expressed in terms of a heparin standard. However, when 10 liters of human blood were extracted by this method in an effort to obtain enough of the material to correctly identify it, all potency was lost. More recently, Monkhouse and Jaques (26) developed a much simpler method for extracting heparin from blood. This method proved not only capable of extracting minute quantities of added heparin but also heparin released by dogs and rabbits suffering anaphylactic shock. Using this method a renewed attempt was made to extract heparin from large quantities of beef, human, rabbit and dog blood.

Results were negative. These authors concluded that if there is a normal heparin in blood it must be less than 0.01 units per ml.

Indirect Estimation

Several workers have attempted to make heparin's affinity for basic substances such as toluidine blue (14) and protamine (33) an indirect means of establishing its presence in blood. However, the difficulty of measuring clotting times precisely and the fact that toluidine blue and protamine are not necessarily specific for heparin, leave the results of such experiments open to question. For instance, interpretation of the results of Tanturi and Wetzel (33) based on reduction of the clotting time of plasma by the addition of protamine would lead one to conclude that normal plasma contained heparin in amounts up to 0.1 mg. (10 units) per ml. This amount of heparin would render blood incoagulable even in ordinary glass tubes. Evidently this method is measuring something other than heparin. Nevertheless these authors conclude from their results that heparin is the "normal anticoagulant of plasma."

Estimation of normal blood heparin has also been attempted by measuring the antithrombic power of serum. Volkert (34) suggested that 20 per cent of the total antithrombin was probably due to heparin. Gerendas et al (13) using a method for measuring the rate of thrombin inactivation by serum went much farther in their speculation. They state that histamine and heparin are both constantly present in the blood under physiological circumstances and the normal coagulability of the blood is regulated by the histamine-heparin equilibrium. It was fairly definitely shown, however, by Monkhouse et al (27) that the Gerendas method is not specific for heparin but rather it measures a resultant of a number of factors.

An experiment by Conley et al (8) is worthy of comment in this connection. These authors prepared platelet-free plasma by high speed centrifugation and showed that such plasma could be inhibited from coagulating by as little as 0.00025 mg. (.025 units) of heparin per ml. Evidently if there is a normal heparin it must be less than this amount.

Thus it seems fairly safe to conclude that if there is any heparin in normal blood it must indeed be very small and can hardly play any important role as a normal anticoagulant. However, we must bear in mind that normal circulating blood is continually passing through organs which are capable of adding or removing activators or inhibitors of coagulation at a rate consistent with equilibrium and an amount of heparin which would exhibit no effect on blood *in vitro* may play a part under such circumstances.

PATHOLOGICAL CONDITIONS

X-irradiation Syndrome

Since the advent of the atomic bomb a great deal of interest has been revived in the hemorrhagic conditions brought about by total body radiation. Allen et al (1) published a paper in 1948 in which they used the term "heparinemia?" Their evidence that the hemorrhagic tendency in the dog was due to the presence of an anticoagulant "indistinguishable from heparin" was based on reduction of the excess clotting time with toluidine blue and protamine sulphate. From the blood of some of

these dogs they succeeded in extracting an amorphous powder with anticoagulant properties. The clotting times of these animals was raised from two to five times the average normal (17 min.) obtained by their method on 13 preradiated animals. They express the potency of the extract as 110 u/mg. but it is not apparent from their data whether this is anticoagulant potency, as their method of assaying the extract is not given. If it is anticoagulant potency it is difficult to see how it could be anything else than heparin, for it would then be equivalent in potency to the best grade of commercial beef heparin. On the other hand, on this basis, the amount of heparin would be at least 10 times the amount necessary to raise the clotting time to the degree found. This was a puzzling situation which the authors indicated by interrogating the title word "heparinemia?" Unfortunately, however, the question mark has been disregarded by subsequent authors and reviewers and has led to the unwarranted assumption by many that heparinemia is a typical finding in radiation sickness. In a more recent article Allen et al (2) have emphasized that the appearance of an anticoagulant occurs in only some of the animals and that the inhibitor is not enough like commercial heparin to be thus classified. Other workers, Rosenthal and Benedek, (30) Rekers (29) and Cronkite (9) have failed to find any significant increase in clotting time or evidence of heparin in the blood.

As already indicated, it is becoming increasingly evident that estimation of heparin based on toluidine blue or protamine titration may lead to serious error. To emphasize this, one has only to recall the report of Honorato (18) in which, on the basis of protamine titration of the blood of choline deficient rats, he arrived at the fantastic figure of 35,000 units of heparin per kilogram of rat. Allen at al (3) have shown considerable increase in protamine or toluidine blue titration in many pathological states associated with hemorrhage as well as in radiated dogs. They state that the bloods of patients and dogs with these disorders rarely inhibit coagulation of normal bloods, and emphasize that factors responsible for the protamine titration in these conditions need not necessarily be heparin or even "heparin-like".

The development and improvement of a sensitive method for extraction of heparin from small quantities of blood has enabled the author to use a more direct approach in examining the blood of radiated animals for this substance. Through facilities extended to us by the Toronto General Hospital (and in collaboration with Dr. E. A. Sellers and his assistant, J. C. D. Barlow) rabbits, guinea-pigs and rats have been subjected to acute radiation. Technical difficulties have so far made it impossible to carry out acute radiation experiments on dogs, but chronic radiation in fatal amounts has been administered to a number of these animals. Moreover, Dr. Garrott Allen of the Department of Surgery, University of Chicago, went to considerable trouble to send us 300 ml. of plasma from one of his animals in the terminal phase of radiation sickness. Although this animal showed an increased clotting time and increased protamine titration we were unable to extract any heparin. Similarly we have so far been unable to extract heparin at any time from any of the radiated animals although many of them showed

evidence of hemorrhage. While it would be premature to conclude from these experiments that heparin is not present at any time in the blood of radiated animals, they do strongly suggest the unlikelihood of it being an important contributing factor to the hemorrhagic manifestations. At the same time, experiments of Fidlar and Monkhouse (11) indicate that it is possible, by means of chronic radiation, to maintain the platelet count of dog's blood below 50,000 for several weeks without evidence of hemorrhage. Thus, thrombocytopenia alone cannot be responsible for the bleeding. As Cronkite (9) suggests, it is more likely a result of combined thrombocytopenia and vascular damage. From our results vascular damage would seem to be of greater importance.

Leukemia

Leukemia is another blood disorder which is often associated with hemorrhage. According to Barnard (4), (5) the hemorrhage in this condition is also caused by increased concentration of blood heparin, though in these publications he presents no data which would substantiate his claim. Rosenthal (31) has divided patients with leukemia into two groups according to their "heparin clotting time" (sensitivity to added heparin). The first group includes patients with normal sensitivity (heparin clotting time under 40 min.) while the second group includes those patients with hypersensitivity to heparin. Eight out of eleven patients in the second group showed clinical evidence of bleeding and five showed a heparin clotting time of over two hours. The interesting point is that all patients, including bleeders, had normal clotting times (6-9 min.) before the addition of heparin. It is difficult, therefore, to imagine how this hypersensitive blood could contain any heparin normally without having a significant effect on the clotting time.

SUMMARY

The foregoing discussion is based on a review of pertinent literature and personal investigation. With the possible exception of certain cases of suggested human anaphylactic shock, (12) there would seem to be too little concrete evidence to justify the clinical use of the terms "heparinemia" or "heparinoid" at the present time. However, while it is proving exceedingly difficult to show conclusively that heparin *is* present in blood, either normally or in clinical cases of bleeding, it will be much more difficult to prove that it *is not* present.

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SOME MEDICAL ASPECTS OF ATOMIC WARFARE*

HUGH CLELAND, M.D.

The material presented in this paper is drawn almost entirely from information made available during a course of instruction on this and related subjects conducted by the U.S. Navy at the U.S. Naval Medical Centre in Bethesda, Maryland.

There is, of course, still a great deal of necessary secrecy about technical details of atomic weapons but effective counter measures in atomic warfare cannot be developed if our whole population is paralyzed with fright or filled with the fatalistic resignation at the mere mention of atomic warfare. Doctors and medical students must have some knowledge about the atomic bomb and the medical aspects of an atomic explosion. You may expect the public to turn to us for information if not actual leadership. We must know the limitations as well as the potentialities of an atomic explosion.

Let us study some of the more important features of atomic warfare learned from consideration of the problem as presented at Hiroshima in August 1945.

If we assumed that Toronto was adequately prepared for defence and contained an organized and well educated public, even with what little we know today, we could reduce the casualties of an atomic bomb to several thousands. This is far better than approximately one hundred thousand casualties which resulted from the bombing of Hiroshima.

The casualties may be divided into three categories: blast, burns and radiation.

BLAST

What was the magnitude of the blast? It was roughly equivalent to 20,000 pounds of T.N.T. and the bomb was exploded at a certain distance above the ground to give the maximum blast effect. Near the centre of the detonation, pressures exceeded 30 pounds per square inch. This pressure would destroy our strongest buildings. Most of the Japanese buildings could withstand only 2 pounds per square inch.

What were the casualties from the blast at Hiroshima? The direct blast effect from the bomb at detonation was rather insignificant and produced about one hundred ruptured ear drums. Humans can apparently survive terrific blast pressures. No ruptured viscera as traumatized lungs were reported. The indirect effects of the blast were tremendous and were manifested by flying debris. Windows were broken 20 kilometres distant. Serious injuries occurred but no effort was made to evacuate the injured and those who could not walk were burned to death.

Failure to rescue thousands of wounded people must not happen here. The public must be given the true facts about the measures which can be taken to minimize casualties and suffering. We must not allow people to be so frightened that they will refuse to participate in rescue attempts. The greatest fear that is generally entertained is that of lingering lethal radiations that we cannot hear, see, smell or taste. Note

*Presented in part to a staff meeting Dept. of Pathology, April 16, 1950, Banting Institute, University of Toronto.

this; less than three minutes after an atomic bomb explodes IN THE AIR, you can enter the centre of the scarred area without receiving a damaging exposure to ionizing radiation.

BURNS

We next consider the burn casualties which were of two types: flash burns and flame burns. Flash burns resulted from the tremendous flash of heat released at the instant of detonation of the bomb. Burns occurred within a short space of time on the exposed surfaces of the body of individuals who were in the open out to the distance of approximately 4000 yards. Clothing offered considerable protection against these burns outside 1000 yards. Light-coloured, loose-fitting clothing gave amazing protection and severe burns occurred only on exposed parts and beneath tight seams, etc. Burns were of all degrees—first, second and third—depending on the distance of the individual from the centre of the explosion.

The effects produced by ultra-violet light were minimal because most of it was absorbed by the ozone emitted in the explosion. Nevertheless, some interesting skin effects did result from ultra-violet light. In some cases the pigment layer of the skin was stimulated and produced the "mask" of Hiroshima. In other cases injury to the pigment layer produced albino-like skin. The flash from the bomb was tremendous and caused temporary blindness in some individuals.

Flame burns from secondary fires were numerous and were caused by overturned stoves, ignited gas mains, and short circuits, etc. The number of flame burn casualties resulting from these fires was tremendous. Serious consideration must be given to the mass treatment of burns. Think of Toronto hospitals suddenly having to handle 75,000 thermal burns. Boston was barely able to care for the some 300 Cocoanut Grove casualties. The first and paramount task is the prompt evacuation of the wounded. Mass hysteria of the populace would be disastrous and would cause greater dislocation of a city's organization than the explosion. If an Atomic Bomb exploded over San Francisco and all survivors jumped in their cars and fled the city, bumper to bumper, by one main highway, the last car would not have left San Francisco when the first car arrived in Salt Lake City, Utah, 700 miles away.

RADIATION

Ionizing radiation is the additional hazard which makes the "A" bomb different from the conventional bomb. Let us not underestimate the radiation hazard which caused 9000 deaths in Hiroshima; but bear in mind that 85 per cent of the total fatalities were blast and thermal burn casualties and would have died if no ionizing radiation had been present. You will almost certainly receive a lethal dose of radiation if you are within 1000 yards of the detonation. Do not let this trouble you. You will likely die from blast or burns.

The balance of this presentation is devoted to the radiological hazards of an atomic bomb. To understand these hazards we must know something about the bomb itself and we must recall certain physical facts about ionizing radiation.

DEVELOPMENT OF "A" BOMB

During the 1930's it was found that bombarding natural occurring uranium

produced a large amount of energy and the possibility of harnessing this energy promoted intensive study. It was found that natural uranium consisted of 99.3 per cent of U238 and only 0.7 per cent U235. Fission of uranium was found mainly to be fission of U235 and that U238 only served to slow down the reaction. Analysis of U235 fission suggested the possibility of a self-sustaining branching chain reaction. By this time it was 1939 and Prof. Einstein wrote his famous letter to President Roosevelt suggesting that intensive research be undertaken to investigate the possibilities of using the fission of U235 as a source of energy for military application. This letter resulted in the formation of the "Manhattan District" with plants at Oak Ridge, Tennessee, and laboratories in many educational centres. What then took the time until July 16, 1945, when the first atomic explosion occurred on this earth?

Purification of U235

Unfortunately we cannot produce a self sustaining chain reaction in natural Uranium because the two neutrons that are produced, and which we hope will sustain the chain reaction, will probably be absorbed by the U238. (For simplicity of presentation 2 is chosen for the number of neutrons produced by bombarding a Uranium atom with one neutron. The actual number is a secret.) Therefore the first and greatest problem facing the "Manhattan District" was to produce a relatively pure source of U235 in order to increase the chances of sustaining a chain reaction which would release tremendous energy and result in an explosion. The obvious solution was to separate U235 and U238. Remember, however, they are isotopes and therefore are not separable by chemical means. Physical methods had to be found based on the slight differences of atomic weight. The two methods that were finally put into operation required the fabrication of huge industrial plants and the solving of fantastic engineering problems. The number of precision instruments for the recording and controlling of temperatures, pressures, flow rates, and so on, in the Oak Ridge plant exceeds the number installed in all other new industrial plants in the United States during the war. To illustrate the magnitude of the problem, consider the obvious method of centrifuge separation. To produce one kilogram of U235 per day requires 22,000 separately driven high speed centrifuges developing forces more than a million times greater than gravity.

Critical Size

Let us assume that this problem is solved and we have a method of obtaining relatively pure U235 even if it is fantastically technical, laborious and expensive. Next let us assume that all other impurities which might interfere with the chain reaction have been removed. The next problem is to prevent our sustaining neutrons from escaping from the surface of the reacting mass and so stalling the chain reaction. The answer is to use a larger volume of reacting mass so that more neutrons are created by the fission of U235 than are lost by escape through the surface of the material. This is possible because the volume of material increases as the cube of any characteristic dimension, say $(L)^3$, whereas the surface increases only as the square $(L)^2$. By increasing the reacting material we eventually

reach a size for which the number of neutrons being produced by the fission of U235 is just balanced by the number lost to U238, to non-fission of U235, to impurities and to the air. This is the critical size. If we increase the size even an infinitesimal amount our reaction is self-sustaining and an atomic explosion is possible.

All this serves to illustrate a few of the tremendous problems that were overcome. Imagine the excitement of H. J. Oppenheimer and his workers at this stage. It was now possible to attack the problems of actually building an atomic bomb. The methods used to assemble and detonate the bomb are top military secrets but certain conjectures can be made.

"A" Bomb Mechanism

A supracritical mass of uranium would detonate spontaneously, the reaction being started by stray neutrons which are always in the atmosphere as a result of cosmic ray activity. Therefore we must start with two or more pieces of subcritical size, and bring these pieces together at the proper time in a short interval. This time interval must be small enough to insure that the parts of the bomb will not be blown apart by the reaction they initiate before the reaction has been able to proceed to some extent. Let us assume that we have two pieces of less than critical size, their combined mass and shape being more than critical size. If these pieces are separated by an air gap of 1 cm., there will be a sufficient number of neutrons escaping to prevent the chain reaction starting. It can be calculated that the masses must be brought together across this 1 cm. in a micro second or less. This involves velocities of the same order of magnitude as projectiles from military guns. Finally we must have an encasement around the critical mass called a "tamper". This must be of sufficient density to hold the reacting mass together for a short time before the supracritical mass blows itself into many subcritical masses and therefore halts the reaction.

Bomb Efficiency

Despite all these efforts it is well known that the Hiroshima bomb was very inefficient. It liberated only the equivalent energy to 20,000 pounds of T.N.T. This is theoretically obtainable from the fission of only 5 pounds of U235. The amount of material in the bomb is considerably greater than 5 pounds. Further research will no doubt be directed at increasing the bomb's efficiency.

"H" BOMB

I can only make passing mention of the fearful "H" bomb which has received so much publicity. We should at least know three things about it. (1) None have been made and perhaps none will be made because of certain practical difficulties. For example, terrific activational energy is required to produce this theoretically possible fusion explosion. A "conventional" atom bomb might even be necessary to explode the "H" bomb.

(2) It is true that a fusion bomb would be much more powerful than a fission Uranium bomb but remember this—the blast range increases only as the cube root of the power of the bomb. In other words, a bomb must be eight times more powerful to produce twice the blast range.

(3) It may be decided for these and other reasons that it is strategically and tactically useless to produce an "H" bomb.

RADIOLOGICAL HAZARDS

Types of Radiation

Following the detonation of an atomic bomb, ionizing radiations are liberated by different processes. Radiations from the bomb may be divided into four categories, namely prompt, delayed, residual and induced. Prompt *gamma* rays are emitted accompanying the nuclear reaction resulting in the detonation of the bomb. The gamma rays from the fission products in the rapidly rising clouds that follow the explosion are known as delayed *gammas*. They can produce severe biological damage for only about 90 seconds after the detonation. The delayed gammas contribute approximately 95 per cent of the total dose to which an individual may be exposed following the detonation. Thereafter, the radition comes from the fission products which fall out of the cloud and is known as the residual radiation. Induced radiation is the radio activity produced by the bombardment of certain elements by the neutrons released at detonation. Neither the residual nor the induced radiation was significant at Hiroshima.

As far as a detonation is concerned, the nuclear particles and rays of biological importance include the *alpha* particle consisting of two protons and two neutrons (a helium nucleus); the *beta* particle, which is an electron; the gamma ray, which is similar to the X-ray; and the neutron which has the mass of a proton but no charge.

Ionization

We are now concerned with the biological effects of these radiations. No doubt you have frequently heard reference to the term ionization as applied to the biological effects of radiation. Ionization can be understood if one considers an alpha particle, a beta particle, gamma ray, or neutron colliding with an atom and thereby causing the atom to lose an electron from its orbit. The ejected electron, since it is negatively charged, is referred to as a negative ion, and the remainder of the atom (less the electron) is referred to as the positive ion. This process is termed ionization. When the atoms comprising a living cell undergo a specific degree of ionization the cell dies.

Ionization Potential

The various radiations have greatly different ionizing power and also greatly different tissue penetration power. Each radiation, therefore, produces the same qualitative effect but their quantitative effects vary enormously. Thus, because of the different ionizing power and tissue penetration power, the actual hazards of the various radiations are vastly different. The alpha particles do not have the ability to penetrate the skin and hence externally present no problem. They are stopped by thin paper or the horny layer of the skin. Beta particles can penetrate only about 0.5 centimeters of skin and 15 meters of air. If present in sufficient quantity, they can produce severe skin damage. Now it must be remembered that radioactive material may be inhaled, ingested, or enter through wounds, and thus cause tremendous havoc. Alpha particles emitted from internal material

may cause damage although they are no hazard on the skin. Therefore, attention must be given to the hazard of internal radiation as well as the hazard of external radiation. However, take comfort from this; internal radiation in atomic warfare is a small hazard and can be fairly easily controlled, for example by such simple measures as wearing an ordinary gas mask.

Gamma rays and neutrons both have the ability to penetrate the skin and deeper structures and cause ionization within the tissues which may result in death. These ionizing radiations are the greatest radiological hazard of an atomic bomb burst in the air. Radiations are emitted at the instant of the detonation of sufficient amount and range to cause lethal effects from 1000 to 1500 yards. These radiations are also emitted from fission products in the rising cloud after the explosion but only in effective range and concentration for less than one and a half minutes following the explosion. Thereafter, the residual and induced radiation hazard are relatively minor and controllable. Rescue teams can certainly pass through the centre of the bombed area. One thing must be made clear: We have been considering the radiological hazards of an air burst. It is tactically the most valuable because of the blast effects and so it is most likely to be used. However, the bomb may be exploded on the ground or under water. If so, the residual and induced radiation hazard will be very much greater.

What follows is a brief summary of the most important features of the biology and pathological anatomy of total body irradiation.

BIOLOGIC EFFECTS OF RADIATION

1. The effects of radiation depend on whether the whole body or only part is radiated. Fifty roentgen units of radiation to the whole body may give symptoms of radiation sickness, whereas a patient may receive fifty roentgen units during a gastro-intestinal series and this causes no trouble because it is directed to the abdomen alone. If a group of humans receive 500 R of total body radiation, one half will die (lethal dose 50 = 500 R).

2. The quantitative biologic effect depends on the type of radiation i.e. Alpha, beta, etc.

3. The more highly developed the organism, the more sensitive to radiation. The amoeba can survive a dose many times the size lethal to man.

4. Different species show different sensitivity to radiation.

5. There are cellular differences in sensitivity and these are important in understanding the clinical picture and pathology of radiation sickness. The most sensitive cells are short lived and actively proliferating e.g. leukocytes, germinal epithelium and intestinal mucosa. The most resistant are static cells such as muscle and ganglion cells.

6. All cells are inhibited and die with an overwhelming dose of radiation.

7. Death of more susceptible cells dominate the picture with a smaller dose.

8. There are certain delayed biologic effects of total body irradiation. The effect causing the greatest dread among the laity is the danger of congenital monstrosities in future children. This is a fearful thought but it seems that total

body irradiation sufficient to cause congenital abnormalities in future children is more likely to cause sterility or death to the parent.

Pathology

The chief features are (1) Hemorrhage and necrosis affecting organs of rapid growth particularly the intestinal tract and bone marrow. (2) Infection secondary to leukopenia.

Radiation Sickness

The clinical features can be reasoned from a knowledge of the biologic effects and the length of survival. The latter depends on the dose of irradiation which in turn depends on the distance from the bomb explosion.[1]

[1]For details, consult:
Shields Warren: Acute Radiation Syndrome in Man. An. Int. Med. 32: 207, 1950.

CONCLUSION

The salient features of atomic warfare have been presented as envisioned from a study of the Hiroshima bomb burst.

This has been done on the premise that counter measures must be developed against the atomic bomb, and the first step is a knowledge of its potentialities and its limitations.

However we must not allow ourselves to become tolerant of the idea of atomic bombs. We must not lose our sense of human values in considering a possible atomic war in merely quantitative terms.

It is a dreadful commentary on the state of human affairs that we must prepare for atomic warfare as a real possibility. But such is the case, because those ruling a large part of the world have shown no genuine will to accept effective controls.

ANSWERS TO PROPER NAMES QUIZ (Page 23)

1. Osteopetrosis (marble bones)
2. Thromboangiitis obliterans
3. Adrenal cortical hypofunction
4. Splenomegaly of undetermined origin
5. Regional ileitis
6. Pituitary basophilism
7. Epidemic encephalitis
8. Leprosy
9. Congenital megacolon
10. Compression fracture of vertebra
11. Osteochondritis of capital epiphysis of femur
12. Cerebral spastic infantile paralysis
13. Dwarfism and infantilism
14. Paralysis agitans
15. Tuberculosis of vertebra
16. Multiple neurofibromatosis
17. Hypopituitary cachexia
18. Amaurotic familial idiocy
19. Thrombopenic purpura
20. Spirochetal jaundice

HUMANISM AND MEDICINE

H. B. VAN WYCK*

PART XVIII

THE 18th CENTURY AND THE TWO HUNTERS

The 18th century evoked a distinct phase in the evolution of philosophic and scientific thought. The century has been called the "Age of Reason" or the "Age of Enlightenment" (Aufklärung). It was the age of theorists and system makers, especially in politics and medicine. Many were the proponents of new doctrines. These sought to bring the results of the new experimental studies and the revelations of science as to the nature of things to the solution of the most important problems of life. The basis of these new ideas was two-fold—now founded on actual research; now on metaphysical speculation. At first, the philosophers predominated in influencing the direction of progress. Such were Rousseau and Montesquieu. Emmanuel Kant and his successors, Fichte, Schelling and Hegel, believed that the origins of science were a priori and could be found in the human intellect. This type of thought prevailed throughout the century. Essentially it held that everything could be explained by a systematic and appropriate reasoning process. While this attitude undoubtedly influenced and retarded the development of medicine; nevertheless, the impetus to experiment persisted in the exact sciences; these and consequently medicine more and more came to regard man as part of nature and to resist the fixed dogmas of scholasticism and metaphysics whenever they tended to halt the rational empiricism without which science cannot advance.

In the midst of these appeals to reason appeared one of the most important among the philosophers, David Hume (1711-76). His rejection of the principle of induction seemed to prove that pure empiricism is not a sufficient basis for science. Hume's scepticism has posed a problem for philosophy. His refutation of rationalism was followed by anti-rationalists such as Rousseau, and later on, Schopenhauer and Nietzsche. The principle of induction cannot be based on inference from observed uniformities since such inference requires the principle of induction for its own justification. Therefore induction must be a principle independent of experience. If this is allowed, then the causal inferences upon which science depends, while perhaps not giving absolute certainty, are sufficient for the unimpeded advance of research in natural science. While these cosmic problems have occupied the interest of the metaphysician during the past two centuries, the natural scientist has ploughed his own furrow. And whenever he has placed his trust in empiricism, his results have borne fruit.[1]

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[1]For a complete and enlightening discussion of the relation of Hume's scepticism to scientific method, the reader is referred to Bertrand Russell's "History of Western Philosophy."

Before the end of the century the intellectual and scientific changes had begun to sharpen the tools of the craftsman in engineering, agriculture, and manufacturing. This change ushered in the Industrial Revolution. Similarly, the application of philosophic thought to the practical problems of politics ultimately led to the beginning of the struggle for the rights of the common man against vested economic and hereditary oppression. The two revolutions are still continuing in parallel courses to the present.

The general political tenor of the century before the outbreak of the French Revolution in 1789 was set by the formal reasoners, theorists and system makers. That the greatest scientific progress of the century was achieved, however, in physics, chemistry, and invention, is attested by the names of Laplace, Cavendish, Priestley, Levoisier, Galvani, Franklin, Watt, Fulton, and Stephenson.

In medicine, the elaboration of the various unsound systems might obscure the fact that the foundations upon which modern medicine has been built were being laid. There were these two groups who directed the progress of medicine in the 18th century: those who were influenced by mysticism, theory, and philosophical speculation; and those who, relying on observation and experiment, directed medicine towards positivism and materialism. The distinction between these is not always clear, but the latter had fortunately a greater and more permanent influence on medical thought. Before the end of the period it was concluded that a complete understanding of the human organism cannot be achieved without the study of its anatomy, physiology, and bio-physical and bio-chemical phenomena. These principles were established because among the many ineffective theorists there were a few original minds like Morgagni, Jenner, Wolff, Hales and the Hunters; and one turns gladly from the theory makers such as Stahl (1660-1734) with his "animism", or Cullen (1710-1790) and "nerve force", to their greater contemporaries.

Prominent among those who kept the Hippocratic tradition alive and laid foundations upon which the great structure of modern medicine could be reared, were the two Hunters, William (1718-83) and his more famous brother, John (1728-1793). Of sturdy middle class Scottish stock, both were born at Long Calderwood, Scotland. William, by ten years the older, came to England in 1740 and began as assistant to Smellie in London. In 1750 he received the medical degree from the University of Glasgow. He became Surgeon-Accoucheur at the Middlesex Hospital in 1748. Having begun early to achieve a great reputation for teaching surgery and anatomy, he successfully combined an illustrious career as a teacher of anatomy with a lucrative practice in obstetrics. In 1770, he provided himself with a house with lecture and dissecting rooms in Great Windmill Street. Here he practised, lectured and dissected; and here he stored his collection of anatomical preparations. This collection and a fine library with an endowment of £8,000 became by his will the property of the University of Glasgow, where the collection may today be seen. Popular with an aristocratic clientèle, and honoured by such appointments as Professor of Anatomy to the Royal Academy and physician-extra-

ordinary to her Majesty, Queen Charlotte, William Hunter remained a man of frugal habits and untiring industry. The most famous English anatomist of the century, in addition to many shorter contributions, he published "Medical Commentaries", 1762; his greatest work "The Anatomy of the Gravid Uterus", 1774. Posthumous works are: "Two Introductory Lectures", 1784, and "Anatomical Descriptions of the Human Gravid Uterus", 1794.

The development of anatomy had been somewhat slower in England than on the Continent. Organized provision for the study of anatomy by observation in England had begun in 1540 when Henry VIII incorporated the Barbers and Surgeons of London into a united Company. The act of incorporation granted to the Company that "they and their successors yearly may have four persons put to death for felony for anatomies". Under Elizabeth, a similar provision for two bodies was granted to Cambridge. It was illegal for anyone to dissect a human body without such official permission. At the dissolution of the United Company of Barbers and Surgeons in 1745, the legal restrictions to private dissection ceased, but the difficulty of obtaining subjects for dissection severely limited the teaching of anatomy. The demand for more surgeons during the Seven Years' War led to the legal provision in 1752 for the dissection of all persons executed for murder in Great Britain. Henceforth the teachers of anatomy, especially those who taught privately, no longer had to depend for the most part on models, casts and diagrams.

Meanwhile, the practice of body snatching had become so prevalent that the University of Cambridge published an ordinance to punish any student or graduate for participation in stealing bodies. The public feeling in Great Britain against dissection was aggravated by the desecration of churchyards and accounted for the backwardness of British anatomical teaching as compared with the schools on the Continent. The poet Shenstone felt impelled to voice popular indignation:

"Where is the faith of ancient Pagans fled?
Where the fond care the wandering waves claim?
Nature instinctive cries, 'protect the dead,
And sacred be their ashes and their fame.' "

Even as late as 1783, William Hunter found it necessary to instruct his students that "in a country where liberty disposes the people to licentiousness and outrage"; and where private anatomists "are not legally supplied with dead bodies, particular care should be taken to avoid giving offense. Therefore, it is hoped that you will be on your guard; and, out of doors speak with caution of what may be passing here, especially with regard to dead bodies." It was thus necessary "to shut our doors against strangers."

In the introductory lectures of his course, William Hunter has left an interesting summary of the status of the anatomical teaching of his times. "In the latter part of the seventeenth century," says William Hunter, "Anatomy made two great steps, by the invention of injections, and the method of making what we commonly call preparations. They arose in Holland under Swammerdam and Ruysch, and afterwards in England under Cowper,

St. André, and others, where they have been greatly improved. The Anatomists who have excelled in making fine injections and preparations have generally made a secret of their methods and improvements, till within the last thirty years (i.e. since 1750) these arts have been constantly taught in public courses of Anatomy here. Harvey and the Anatomists of former ages had no other knowledge of the blood-vessels than what they were able to collect from laborious dissections, and from examining the smaller branches of them upon some lucky occasion when they were found more than commonly loaded with red blood. But filling the vascular system with a bright-coloured wax enables us to trace even the smallest vessels. The modern art of corroding the fleshy parts with a menstruum, and of leaving the moulded wax (in the vessels) entire, does great honour to the ingenious inventor Dr. Nicholls.

"Many of the wax figures which I have seen are so tawdry, unnatural in colour, incorrect in figure, situation, and the like, that to an Anatomist they appear ridiculous. But those which are cast in wax, plaster, or lead, from the real subject, and which of late years have been frequently made here, are very correct, and are no insignificant acquisition to modern Anatomy. The improved methods of preserving animal parts have been of the greatest service, either wet preparations in spirits, or dry preparations covered with protective varnish: of the two the former being preferable, inasmuch as they retain more of the natural appearance. But they can never take the place of the fresh subject.

"The large folio illustrations of the bones, the muscles, and the blood-vessels, as well as those of the internal organs of the body, have facilitated the study of Anatomy: but none of these artificial means are capable of taking the place of the human body in the proper instruction of the student."[1]

There had been a succession of private extra-collegiate teachers of Anatomy since 1700. They had been severely handicapped by legal restrictions and lack of subjects. By them, however, the foundations were laid and the later work of William Hunter made possible. He was fortunate in beginning his work about the time of the dissolution of the United Company of Barbers and Surgeons (1745) and the consequent repeal of their by-law against extra-collegiate dissection. A few years later (1752), when the larger number of subjects was provided by Act of Parliament, Hunter's school became without rival. Among those whom he taught were the leaders of the next generation, some of whom carried his wisdom and spirit to the new world. Lecturing was to William Hunter a great joy and in spite of his many other professional distractions, he continued his courses. As he said, he "conceived that a man may do infinitely more good to the public by teaching his art than practising it."

Matthew Baillie, his nephew (1761-1823), himself the author of the first systematic text on pathological anatomy in any language, speaks thus of William Hunter: "No one ever possessed more enthusiasm for his art, more persevering industry, more acuteness of investigation, . . . or indeed a greater share of eloquence. . . . He was, perhaps, the best teacher of anatomy who ever lived." "To him, Anatomy owes a debt in some

[1] "A Memoir of William and John Hunter," William Brendon & Son, Plymouth. 1824.

measure comparable to that which Pathology owes to his brother."[1]

Indeed, no small part of the fame of William Hunter is due to the generous help he was able to render the career of his younger brother, John, an incomparably more comprehensive and original genius. John Hunter, in contrast to the urbane William, a rougher diamond, had a more chequered and romantic, though stormy, career. Eventually, however, his intense genius, overpowering will, and devotion to work made him one of the greatest figures in English medicine. To summarize, an indefatigable dissector and student of comparative anatomy, he spent his life in emphasizing the importance of investigation and experiment; and, as even more successfully than William, he combined a large practice with scientific study, he may be said to have raised English surgery from a trade to a scientific profession. A tangible monument to his almost incredible industry and single-minded enthusiasm remains in his museum collection of thousands of preparations which to-day can be seen at the Royal College of Surgeons of London. His career ultimately placed him among the greatest biologists of all time, and as one of that supreme trio of surgeons with Paré and Lister. Its beginnings were, however, inauspicious.

John Hunter was born in 1728, the youngest of a family of ten children. By the exercise of great frugality and the impoverishment of his estate, the father was able to offer the usual educational opportunities to the boys. Unlike William, who gave early promise of his later achievements, John until past his teens, remained "a raw, uncouth Scotch lad fonder of taverns and theatre galleries than of book-learning."[1] As he afterwards said of himself: "When I was a boy, I wanted to know all about the clouds and the grasses, and why the leaves changed colour in the autumn. I watched the ants, bees, birds, tadpoles and caddis worms; I pestered people about what nobody knew or cared anything about."[2] In his twentieth year, lured doubtless by the growing fame of his elder brother in London, he wrote to William asking to be allowed to come and work under him. An encouraging answer was received and John was soon at work dissecting and teaching anatomy under William's direction; also studying surgery under Cheselden and Pott at St. Bartholomew's Hospital.

In 1756 he became house surgeon at St. George Hospital for a short period. His health suffering from the intense assiduity with which he pursued his studies, an appointment as staff surgeon to the army gave him a beneficial change of scene as well as a chance to practise surgery. In 1760, he joined Keppel's expedition to Belleisle and the following year he saw service in Portugal. These two years in the army provided part of the material of Hunter's last published work: "The Treatise on the Blood, Inflammation, and Gun Shot Wounds," a publication which did not appear until a year after his death.

In 1763, John returned to London from his war service in the Spanish Peninsula and resumed his unflagging application to anatomical and physiological study. At the same time, he began private practice in Golden Square. Most of the metropolitan practice of the time was held by Caesar Hawkins, Percival Pott, and Samuel

[1]F. H. Garrison: "History of Medicine."
[2]Stephen Paget: "John Hunter."

Sharp; and Hunter sought to eke out his slender income by private tutoring in anatomy and surgery. His main preoccupation in comparative anatomy and pathology did not favour the rapid growth of a demand for his surgical services.

And now began the collection of animals, living and dead, brought from the four quarters of the globe. These he housed in his residence at Earlscourt, Brompton, purchased in 1765. In 1771, John Hunter married Anne, eldest daughter of Robert Home, a military surgeon. This gently nurtured lady has a modest claim to immortality in her own right, inasmuch as she furnished the words for Haydn's English canzonets among which are the lines beginning "my mother bids me bind my hair." How this clever and socially popular woman adjusted herself to presiding over a household which partook more of the nature of a zoological museum can only be surmised. A description of the life in the town house in Jermyn Street where John Hunter moved in 1768 has been left by Everard Home:

"At this time (about 1774), John Hunter's private practice and his professional character were advancing very fast, and his family had begun to increase, but still no small part of his time was devoted to his collection, which, as it daily became larger, was also attended with greater expense. The whole suite of the best rooms in the house was occupied by his preparations; and he dedicated his mornings from sunrise to eight o'clock (the hour for breakfast) entirely to his pursuits. To these he added such parts of the day as were not engaged in attending his patients."[1]

"One morning, finding Mr. Hunter very busy in his collection, Dr. Gartshore observed, 'Ah, John, you are always at work!' 'I am,' replied Mr. Hunter, 'and when I am dead, you will not soon meet with another John Hunter.' "[2]

"On returning home late one evening, after a hard day's fag, Hunter unexpectedly found his drawing-room filled with musical professors, connoisseurs, and other idlers, whom Mrs. Hunter had assembled. He was greatly irritated, and walking straight into the room, addressed the astonished guests much in the following strain: 'I knew nothing of this kick-up and I ought to have been informed of it beforehand, but as I am now returned home to study, I hope the present company will retire.' This intimation was, of course, speedily followed by an exeunt omnes."[3]

But it was at his Earl's Court house where most of his biological researches were carried on and there life was certainly not dull. Here among the rapidly increasing swarms of animals, John Hunter carried on his observations and experiments. "He had never read Bacon," writes G. B. Babington, "but his mode of studying nature was as strictly Baconian as if he had." To Edward Jenner, a pupil and life-long friend and correspondent, he wrote, "I think your solution is just, but why think? Why not try the experiment?"

The correspondence with Jenner, considerable of which has survived, tells us much of Hunter's methods. Many of these letters are taken up by requests for hedgehogs, lizards, frogs, pheasants, and

[1]Life of John Hunter. Sir Everard Home, 1794.

[2]Memoirs of the late John Hunter, Esq. Joseph Adams, London, 1817.

[3]The Life of John Hunter. Jesse Foot, 1794.

other animals. A characteristic letter, after acknowledging the receipt of some blackbirds from Jenner proceeds: "I was told the other day, you was married. I hope it is true. What has become of your paper on lead in cider?" The enormous collection grew steadily and from it Hunter filled "literally a cart-load" of manuscripts with descriptions of dissections, reports of experiments, and detailed notes. In 1785, he moved his collection which had by this time cost him £10,000 into a specially constructed museum containing a gallery and a lecture theatre.

In the meantime, Hunter carried on his courses of eighty-six lectures on surgery delivered on alternate evenings. In these the emphasis was on principles based not only on anatomy but also on pathology. Some portions of these lectures remain extant in the notes taken by pupils; the original manuscripts with other copious memoranda were burned by Sir Everard Home in 1823! In 1768, Hunter was elected a surgeon to St. George's Hospital, and now with professional standing and the prestige won by numerous contributions to the literature of comparative anatomy, pathology, and general biology, honours came fast upon him. In 1776, he was appointed surgeon extraordinary to the King; in 1783, elected to the Royal Society.

Hunter's influence on surgery has been as great as his contribution to pathology. He taught that operative interference was an acknowledgment of the imperfection of the art of healing, and he compared surgery, uncontrolled by cooperation with the "vis medicatrix naturae" to "the acts of an armed savage who attempts to get that by force which a civilized man could get by stratagem." An illustrious example of his viewpoint was his inauguration of a new operation for aneurism. His experiments on the buck had shown that "under the stimulus of necessity, the smaller arterial channels are capable of rapid increase in calibre to perform the functions of the larger." With this in mind, he treated a patient with a popliteal aneurism by ligature of the femoral artery in the space now known as "Hunter's canal" with a successful outcome. Among his more important publications are: "Treatise on Venereal Disease," 1786; "Observations on certain parts of the Animal Oeconomy," 1786; and the posthumous work on "Blood, Inflammation and Gun Shot Wounds." In all these, the application of physiology to practice is fundamental. "When we make a discovery in pathology," wrote Adams in 1818, "We only learn what we have overlooked in his writings or forgotten in his lectures."

With the death of Percival Pott in 1788, John Hunter was now the unrivalled first surgeon of England; but with failing health, he gave up much of his professional activities, and, resigning his lectures to his brother-in-law, Home, he devoted himself to the completion of his writings. For years he had suffered from anginal attacks, the frequency and intensity of which were favoured by his irrascible temper and intolerance of stupidity. To these qualities is due the atmosphere of controversy in which most of his life was lived. It was said that his attitude to his colleagues was overbearing. While he owned himself "a pigmy in Knowledge, he felt a giant compared with them"; and he found himself unable to control his scorn for their lack of scientific enthusiasm, their wish to accept fees for

work they were unwilling to share, and their neglect of what he believed to be their prime duty as hospital surgeons—the teaching of students. Doubtless his colleagues recognized his intellectual superiority, but it was not until his death that the true stature of his prodigious genius was appreciated.

On October 16, 1793, John Hunter died while in attendance at a Board meeting at St. George's Hospital. His remains were deposited in the north aisle of the nave of Westminster Abbey near the grave of Ben Jonson.

The Hunterian collection of over 13,000 speciments was offered for purchase by the British Government; but the Prime Minister, Pitt, refused, exclaiming: "What! Buy preparations! Why, I haven't enough money to buy gun-powder." In 1799, however, the government voted £15,000 and the custodianship of the precious collection came to rest where it now remains, with the Royal College of Surgeons.

A loyal retainer, William Clift, afterwards for years the faithful conservator of the Hunterian collection, wrote this quaint memorandum on his account book:

John Hunter, Esq., F.R.S.
Surgeon-General to the Army, and
Inspector-General of Hospitals;
Surgeon to St. George's Hospital;
Surgeon Extraordinary to the King,
etc., etc., etc.
Died October 16th, 1793.
On the same day, and perhaps hour that
the unfortunate Marie Antoinette,
Queen of France, was beheaded in
Paris.

W. Clift.

JOHN HUNTER'S DAY

Hunter used to spend every morning from sunrise until eight o'clock in his museum, and throughout the day he carried out his extensive private practice, performed his laborious duties as Surgeon to St. George's Hospital, and Deputy Surgeon-General to the Army, delivered lectures to students, and superintended a school of practical anatomy at his own house, finding leisure, amidst all, for elaborate experiments on the animal economy, and the composition of various works of great scientific importance. To find time for this gigantic amount of work he allowed himself only four hours of sleep at night, and one hour after dinner.

Samuel Smiles

ABSTRACTS

MEDICINE

Clinical Variations in Primary Atypical Pneumonia: W. S. Jordon, et al. Amer. J. of Med., **10**: 3-20, 1951.

Detailed studies of 67 cases of primary atypical pneumonia reveal the varied clinical patterns this condition may assume. In the majority, the onset was gradual and the total duration averaged 23.6 days with a range or 7 to 52 days. The chief complaints in order of frequency were cough, malaise and fever. During the course of illness, most had in addition to these sore throat, headache and anorexia.

Abnormal pulmonary signs were absent on admission in 22% but eventually developed in all but two. Fine rales occurred in 91%; dullness, diminished breath sounds and coarse rales each in 50%; bronchial breath sounds in 24% and pleural friction rubs in only two cases. These signs persisted for an average of 21 days after onset with a range of 3 to 52 days.

On admission, 50% showed pulmonary signs corresponding in extent to the degree of involvement as seen by X-ray. In the rest, there were discrepancies, some marked. Leucocyte counts averaged 9,000 and ranged from 4,000 to 35,000, without secondary infection. An increase most often accompanied spread of the pulmonary lesion.

Fourfold or greater rises in titer, either of cold haemagglutinins, of streptococcal M.G. agglutinins, or both, occurred in 65% in direct correlation with the severity of the illness.

M. C. Gerstein

Tuberculosis of the Sacro-Iliac Joint: S. T. Scholt, J. of Bone and Joint Surgery, **33-A**, 119-129, 1951.

Incidence: This is not a rare disease, occurring mainly in young adults, 80% of 75 cases being in the 20-40 age group, the youngest 7, the oldest 57. The race and sex distribution were not a factor and only 7 cases were bilateral. However, 83% had associated lesions, half of these were skeletal and most often the spine.

Signs: 80% first experienced pain in the posterior iliac or hip region while 30% experienced sciatic radiation. 8% had no pain but developed swelling with the formation of an abscess, while 9% had no symptoms. Subsequent abscess formation occurred in 80%, the majority over the sacro-iliac joint or the inguinal region and most of them eventually formed a draining sinus.

Radiographic: Haziness or loss of definition of the joint line occurs early while later one sees irregularity of the articular surfaces with eroded areas. If the disease subsides, a narrowed joint space with adjacent dense bone occurs, but if the disease continues, destruction becomes more marked and cavitation may occur. 90% of cases showed bony ankylosis in 8 years.

Treatment: Tuberculosis as elsewhere is treated as a systemic disease with bed rest, adequate nutrition and immobilization in plaster. The results with streptomycin are still too inconclusive to evaluate. Operative fusion of the joint is of value in hastening bony ankylosis.

Prognosis: Tuberculosis requires lengthy hospitalization and although mortality with antibiotics is decreasing, it is at present around 30%. Of the survivors followed, 80% had no pain or discharge and were wage earners.

E. R. Jones

Oral Steroid Medication in Rheumatoid Arthritis: Freeman, et al. J. Clinical Endocrinology, **10**: No. 12, 1950.

This is a study of the results of oral administration of pregnenolone to 64 patients with rheumatoid arthritis. In the study patients were classified according to the degree of progression of the disease, limitation of functional capacity, and response to therapy. The patients as a whole were middle-aged and chronic sufferers from rheumatoid arthritis with marked anatomical and functional limitations.

Maximum improvement was obtained by a daily dose of 500 mg. of pregnenolone; 400 mg. seemed to be a minimum average daily dose for maintenance of improvement. Time of administration varied from 2 to 30 weeks. As a result of this therapy: (1) 38% showed major improvement as evidenced by lessening of pain and increased functional capacity of limbs and joints; (2) 41% showed similar but less striking improvement; (3) 21% showed no improvement.

Chances of a favorable response varied with the severity of the disease; the worst cases showing the least improvement. The age of the patient bore some relation to improvement. In older groups there were more minor than major improvements. However, the duration of disease bore no relationship to the amount of improvement.

There was a great tendency to relapse after medication was discontinued. Duration of improvement without the drug had a direct relationship to the duration of pregnenolone administration.

Placebo therapy before or after true administration showed very little effect and played a negligible part in any major improvement.

Pregnenolone, then, can be regarded as an aid to treatment of arthritis. It is less expensive than ACTH or cortisone, has no profound toxic or physiologic effects, and its effectiveness by the oral route simplifies administration.

J. B. Redford

Severe Serum-Sickness Type of Penicillin Reaction—Failure of Antihistaminic Therapy: M. Zussman, Annals of Allergy, 8: No. 6, 1950.

By means of many different case reports the author endeavours to persuade us not to sensitize everyone. These cases show that anti-histaminic drugs often have no effect in controlling the more serious penicillin reactions, that the method of administration has nothing to do with the allergic reactions to penicillin, and that the delayed type of serum-sickness reactions may end fatally.

Serum-sickness reactions are of three types: (*a*) delayed—usually occurs seven to ten days after the primary injection; (*b*) accelerated—may occur after several hours and generally after a second injection, giving more violent symptoms; (*c*) local—causes local swelling and tenderness at the site of injection. Severe irreversible tissue destruction may follow serum sickness. Typical lesions of periarteritis nodosa have been demonstrated. Anaphylaxis can occur in guinea pigs as a result of serum sickness.

Allergic reactions occur most frequently in patients who have had several treatments with penicillin. Skin tests are unreliable in predicting these reactions. Because of its ability to sensitize, penicillin should be used only when not to do so would jeopardize the health of the patient.

R. L. Ruderman

Oral Hexamethonium Bromide in Essential Hypertension: Mackey, W. A. and Shaw, G. B., B.M.J. 4726: 259 (Aug. 4) 1951.

Ever since pharmacological research showed that compounds with carbon chains of five or six atoms exerted action at ganglionic synapses, and were capable of influencing the autonomic nervous system, attempts have been made to employ these compounds in the treatment of diseases where hyperactivity of the autonomic nervous system might possibly be playing a part.

The authors investigated the use of oral doses of hexamethonium bromide (C6) in controlling the manifestations of essential hypertension in 15 cases. These patients were treated for from one to ten months, and were given 0.25-0.5g. three times a day, before meals.

Five of these 15 cases have been classified as improved. Considering the blood pressure alone, a reasonably maintained lowering has been achieved in 8; in the others, the effect has been negligible. Three of the improved five previously had hypertension bordering on the malignant phase.

The side effects of which the patients complained included headaches, dizziness and lassitude. All had dry mouths and constipation; a few had anorexia.

The authors conclude that, while the drug is not a cure, it is a means of relieving the symptoms and reducing the blood pressure in certain cases of essential hypertension.

M. L. A. Auerback

SURGERY

Oesophago - Dermato - Oesophagoplasty for Congenital Oesophageal Atresia: D. E. Ross, et al. C.M.A.J., 64: No. 2, 128-131, 1951.

The authors state that congenital atresia of the oesophagus occurs in one in 5000 live births and is one-sixth as common as cleft lip and palate. Most commonly, (90%), the anomaly takes the form of a blind upper segment, with a tracheo-oesophageal fistula of the lower segment. It is believed to be caused by the failure of mesodermal elements to separate completely the trachea from the oesophagus in the early single embryonic tube, and a simultaneous failure of recanalization of a portion of the oesophagus.

Diagnosis is made on the grounds of excessive drooling of saliva or mucous by the newborn infant, associated with immediate regurgitation of ingested food in an unchanged form, and frequent bouts of coughing and syanosis. To establish the diagnosis, a soft rubber duodenal tube is inserted and this will stop short in the blind end. A small amount of lipiodol introduced at this time will show by X-ray the level of the blind segment, and any tracheo-oesophageal fistula with this segment. If a fistula is present between the lower segment and trachea, there will be air in the segment and stomach.

Various surgical approaches are desjunum under the skin of the chest wall to cribed, most of which use sections of jeconstruct a new segment. The operation of choice can be performed when the atretic portion is short enough to permit the direct anastomosis of the blind ends.

The case described is alive and well seven years post-operatively.

R. B. Trewin

Aspiration Treatment of Perforated Ulcers: H. Taylor. Lancet No. 1: 7-12, 1951.

A review of 73 cases of perforated ulcers who were considered suitable for operation but who were treated by the aspiration method is presented.

In early cases, before infection has occurred, the object of the aspiration is to permit closure of the perforation. It is shown that this will close spontaneously if the stomach is emptied promptly and the aspiration is continued preventing any fluid or gas from passing through the aperture. When infection has taken place in the later stages, aspiration is used to prevent re-infection while the toxic fluid in the peritoneal cavity is being removed or absorbed.

The patients were watched closely in case surgical intervention was necessary. A steady rise in pulse rate indicating a virulent infection or an increase in subdiaphragmatic gas (as seen radiologically), indicating failure of the perforation to close, would justify operative procedures.

Of the 73 cases reported, 2 died from the effects of gross air-swallowing with inadequate aspiration, 5 from causes not related to the method of treatment.

In conclusion, the author advises prompt evacuation of the stomach contents by aspiration for the treatment of perforated ulcers, the aspiration being continued until the perforation has closed and surgery being reserved for complications.

R. E. Turner

Treatment of Planter Warts with Elastoplast and Podophyllin: D. A. Duthie, D. I. McCallum. B.M.J., No. 4725, pp. 216-218, 1951.

The histology of the plantar wart explains the rationale of elastoplast treatment. There is elongation of dermal papillae, downgrowth of epidermal pegs. The wart lies below the surface, covered by a horny cap. If the cap is removed, the body of the wart becomes accessible to treatment.

Radiotherapy is advised for the soli-

tary wart only. Mosaic warts (a cluster of small warts) and multiple warts are often treated by diathermy and curettage, with much subsequent discomfort. Surgival excision usually results in a painful scar and recurrence.

The elastoplast and podophyllin treatment is simple, effective, applicable to all types of plantar warts, and can be used after failure with surgery or x-ray. The authors advise the following procedure:

The horny surface is pared down as far as possible without causing bleeding. The cap, however, will soon reform unless prevented from doing so. The application of tight elastoplast macerates the remaining horny material and regrowth is often stopped if occlusion is maintained for several weeks. Every two weeks the debris is scraped away and the elastoplast changed. The application of 25% podophyllin to the macerated wart after the fourth week, with continuation of elastoplast is found to bring about cures in 60% of cases within two months.

Complications to be watched for are sensitization either to elastoplast or podophyllin. Podophyllin usually causes very little dermatitis on the thick skin of the sole, but should be used with caution elsewhere.

S. Hecker

PEDIATRICS

The Use of Ascorbic Acid Tablets to Enrich Milk for Infant Feeding. A. D. Holmes, Ph.D., C. P. Jones, B.S., F. Tripp, M.S. Journal of Paediatrics, pp. 320-324 (Sept.) 1951.

Though milk has been described as nature's most perfect food it is inadequate in iron and ascorbic acid. The amount of ascorbic acid in orange juice which is used to supplement infant feeding has been found to vary from 27 to 67 mg. per 100 cc. This variation in vitamin C content of oranges has been found to depend on many factors: picking date, geographical location, variety of orange and even the position of the orange in the tree. This paper, therefore, discusses the feasibility of adding pure crystalline vitamin C to the infants' milk to insure a uniform and adequate supply of this essential vitamin.

Milk which had been enriched with vitamin C and stored in the dark at 10 degrees centigrade was found to have lost considerable of its ascorbic acid content. At higher temperatures and in sunlight much more ascorbic acid would be lost. It has been found that pasteurized milk in a clear glass bottle at room temperature will lose all its ascorbic acid in six hours. Addition of ascorbic acid to milk in the dairy then, is not feasible. However, it is possible to supply tablets which contain a known amount of the vitamin which are readily soluble in milk. By adding a tablet to the milk immediately prior to feeding, it is possible to insure an adequate concentration of ascorbic acid.

Many studies comparing the synthetic and the naturally-occurring ascorbic acid indicate that the synthetic vitamin is not inferior to the natural vitamin. The American Medical Association in commenting upon the utilization of ascorbic acid, states that synthetic ascorbic acid is absorbed and utilized by the body as well as that from natural sources.

The authors summarize that while oranges will supply vitamin C, they are expensive, cumbersome and variable in their ascorbic acid content. Ascorbic acid tablets, on the other hands, provide a convenient means for adding to the infant's bottle a standardized, uniform amount of ascorbic acid sufficient to meet daily nutritional requirements.

P. Montgomery

DERMATOLOGY

Acid-base Balance of the Skin: D. S. **Anderson:** British J. of Dermatology, 63: 283, 1951.

It has long been known that the normal skin has an acid reaction produced mainly by lactic, formic, propionic, and butyric acids. There is a gradual decrease in pH as one goes from the dermis to the epidermis. The normal averages are between about pH four and six, that of the female being 0.2-0.3 pH units higher on the average.

Using the sealed glass electrode and the Cambridge pH meter, the author carried out a systematic investigation of the pH of the entire integument of 50 normal children with various dermatoses—mainly cases of atopic and seborrheic eczema with or without xeroderma.

In the normals, the pH was found to vary from four to six, the body's flexures giving the highest readings.

The more severe the eczema, the higher the pH was raised. It is interesting to note that the body areas of highest average pH varied for the different types of eczema. In atopic eczema (cases of Besnier's prurigo and facio-flexural eczema of infants) no cause for the increased pH was discovered, but it was shown to be secondary to changes in the keratin layer. In xeroderma, the pH of the ? ? ? ? was raised due to the abnormally small amount of sweat secretion.

Seborrheic eczema shows a tendency to secondary infection, and this tendency is present even after the lesions heal. The pH of the skin in this condition was raised to an even greater extent than in xeroderma. The pH was higher than normal in these patients even after the lesions healed. The cause of the increased pH is primarily due to the altered pH of the sebaceous secretion, and secondarily to the intradermal and intra-epidermal edema. The higher pH seems to predispose the patient to secondary skin infections.

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NEWS AND NOTES

Medical Society

Syd Wax, president of the Medical Society, was unanimously elected as president of the Students' Administrative Council for the year 51-52. We are confident that the ability he has shown in his work for the Medical Society in past years will enable him to fill this responsible position with competence. The position of Public Relations Director of the S.A.C. is being ably filled by Ann-Jane Carter who is also president of the Medical Womens' Undergraduate Association.

* * *

The final meeting of the Medical Society for the year 50-51 was held at the Hearthstone Restaurant. The Dean of Medicine, Dr. J. A. MacFarlane, and Dr. L. J. Rogers, who was elected honorary secretary-treasurer for the Medical Society for the present year, spoke to the past and incoming executives of the Medical Society. A new motto for the school of medicine was adopted at that meeting.

* * *

Even greater efficiency can be expected from the Medical Society this year as a result of the brighter outlook which the Medical Society office now presents. The new curtains and painted walls are a result of the efforts of 1st year president Tom McCulluch. And members of the Medical Society will not longer be distracted during meetings by crooked pictures.

* * *

At the opening meeting of N.F.C.U.S. held on Oct. 2nd, Syd Wax was elected chairman of the International Activities Commission. Syd Wax will attend the Edinburgh International Student Conference in January as the representative of Canadian universities and he will present the Canadian viewpoint on international student problems.

* * *

A sub-committee of N.F.C.U.S. plans this year to investigate the possibility of lowering the cost of text books imported from the United States. It is possible that by decreasing the import tax, reductions of from 10-20% may be obtained.

Congratulations to John Evans who was unanimously elected captain of U. of T. Blues for the present year.

* * *

This year Daffydil Nite, which is being organized by Ted Nugent, will run for five nights—from Dec. 17th to Dec. 21st. The Medical-At-Home is scheduled for Feb. 20th.

* * *

The Medical freshmen were welcomed by Syd Wax and other members of the Medical executive at the Freshman Reception on Oct. 1st. The speakers were Dean J. A. MacFarlane and Dr. Paul McGoey, orthopaedic surgeon at St. Michael's Hospital. Refreshments were served and light entertainment was provided by Barry De Veber and Stan Bain.

* * *

At the conference of the Canadian Association for Medical Students and Internes which was held at Queen's University from Oct. 10th to Oct. 13th, the Medical School of U. of T. was represented by Milt Francis and Terry Doran. We will have more to report about this meeting in the next issue.

* * *

Dr. Gordon Cameron, Dr. Betty Line, Dr. Tony Cecutti, and Dr. Claude MacDonald won the highest honour awarded to undergraduates—the S.A.C. Honour Award. These are given on the basis of the student's contribution not only to his own faculty, but to the University as a whole. Dr. Cameron and Dr. Line were honoured for their capable work in the Medical Society and the S.A.C. Dr. Cecutti was outstanding in University sports activities. Dr. MacDonald was president of the Canadian Federation of Newman Clubs and president of Pax Romana.

* * *

Eighteen graduates of the class of 1901 joined the graduating class of 1951 on June 14th in Hart House for the annual Graduation Banquet. Dr. G. Wright Young, president of the Alumni Association was chairman for the evening. The

guest speaker, Professors H. Wasteneys, spoke to the group on the contributions to medicine made by the teachers of Toronto's Faculty of Medicine. Professor Wasteneys is at present Head of the Department of Biochemistry at the University of Toronto.

* * *

The student undergraduate body was deeply shocked at the loss of Jack Zoberman who was accidentally drowned this past summer.

* * *

The Wm. Osler Society held its first meeting for the year on Thursday, Sept. 28th. Two papers were presented: one by John Evans, the other by Stan Bain. John Evans spoke of Sir Thomas Browne, his life and contributions to the field of medicine; Stan Bain discussed the background of Greek medicine before Hippocrates and the changes wrought by Hippocrates in medical ethics.

* * *

Alec MacIntyre 5T4 was chosen by the Association of Canadian Medical Colleges as the recipient of the Oxford Scholarship. This was the first time that this scholarship had been available to Canadian students. The Oxford Scholarship will enable Alec to study at the University of Oxford during the next five years. He will receive the degree of Bachelor of Arts at the end of two years and his Bachelor of Medicine after five years of study. Alec MacIntyre was president of his class last year and he was to have been treasurer of the Medical Society for the present year.

* * *

ALUMNI

For the first time in its history, the Ellen Mickle Fellowship was won by two

MEDICAL ALUMNI SCHOLARSHIP WINNERS MEET ALUMNI EXECUTIVES

1st row: Dr. E. J. Clifford, Chairman of Scholarship Committee, G. Y. Hiraki 5T3, J. M. Johnson 5T6, E. M. Culp 5T4.
2nd row: G. S. Cohen 5T5, P. H. Melville 5T1, R. F. Brown 5T2.
Standing: Dr. G. Wright Young, President, Medical Alumni Association.

students, Sylvia Ramcharan and Sam Bogoch. The Medical Alumni has very generously donated a sum equal to the value of the scholarship so that both students may benefit fully.

Other Medical Alumni Scholarships were won by: J. M. Johnson 5T6, G. S. Cohen 5T5, E. M. Culp 5T4, G. Y. Hiraki 5T3, R. F. Brown 5T2, and P. H. Melville 5T1.

* * *

FACULTY

At the annual meeting of the Canadian Medical Association, held in Montreal from June 18-22, surgery in progress at the Royal Victoria Hospital was televised to the lobby of the hotel. A radical mastectomy was performed by Dr. R. M. Janes, head of the Department of Surgery, and the only surgeon outside the Montreal area invited to participate in the program.

* * *

Dr. W. R. Harris has received an award from the W. E. Gallie Trust Fund for post-graduate study in surgery. This is the first year that this award has been made and Dr .Harris is using it to continue his work in orthopaedic surgery in Boston.

* * *

Dr. R. M. Janes delivered the Arthur Dean Bevan lecture before the Chicago Surgical Society on Oct. 5. His subject was "Surgery and Bronchiectasis."

* * *

Dr. R. I. Harris has retired as Associate Professor of Surgery and Chief of the Orthopaedic division of the T.G.H. However, students will be glad to hear that although he has retired from active conduct of the division he will remain active in undergraduate and post-graduate teaching. Dr. F. P. Dewar will replace Dr. Harris.

* * *

Plans are under way for modernizing the Toronto General Hospital and these include new lecture rooms and common rooms for the students. More detailed information about these plans will be available in the near future.

* * *

Four members of the Department of Surgery have been in Paris attending the convention of the International Society of Surgeons. They are Drs. R. C. Laird, A. W. N. White, F. B. Plewes, and W. G. Bigelow.

* * *

Dean J. A. MacFarlane has been elected president of the Association of Canadian Medical Colleges.

* * *

Professor A. M. Wynne has been appointed head of the Department of Biochemistry and Dr. Charles Hanes, at present at Cambridge, is expected to join the department later in the fall. Professor Wynne succeeds Dr. H. Wasteneys who retired from active leadership of the department last June.

* * *

A new program of decentralized post-graduate medical education has been announced jointly by the University of Toronto and the Kellogg Foundation. Three Ontario centers, Kirkland Lake, Fort William and Port Arthur, and Port Colborne have been chosen to initiate this program. Teams of clinicians will be sent out to each area where they will hold clinics in the hospitals on patients presented by the local physicians. Six sessions are to be held in each center, and it is hoped that such instruction will be of more benefit to the practising physician and less time-consuming than similar courses given in one large center.

* * *

A native of British Columbia, Dr. John D. Hamilton, the newly appointed head of the Department of Pathology received his degree in Medicine from U. of T. in 1935. He interned at the Toronto General Hospital and spent a year studying pathology with Dr. Boyd. He went from Toronto to Cambridge where he spent two years and from there he went on to Baltimore. During the Second World War he was overseas with the Canadian Army Special Field Research Unit. On his return he joined the Pathology Dept. at McGill University and from there he went to Queen's where he headed the Pathology Dept. At present he lectures in General Pathology to the second medical year.

MISS J. GRIFFIN.
MISS D. LIEBERMAN.

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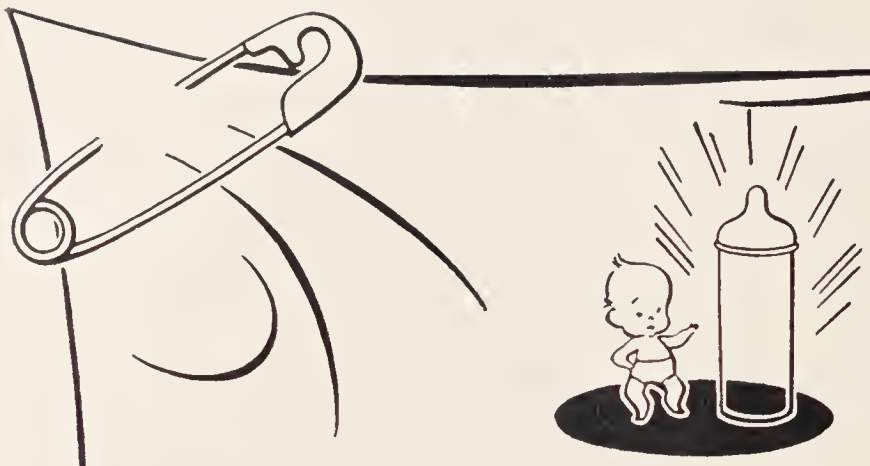

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1. Am. J. Obst. & Gynec. 54:738 (Nov.) 1947.

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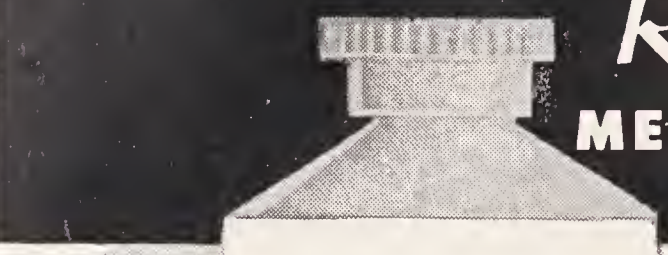

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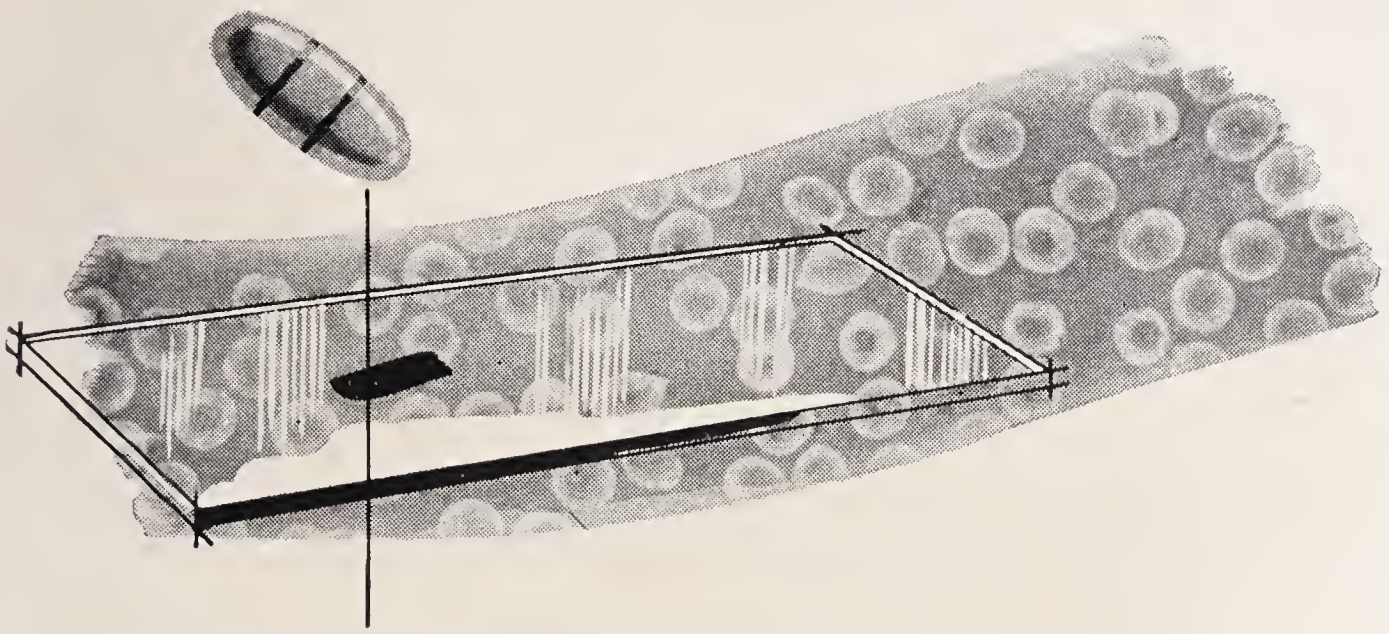

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